

## Summary of Safety and Clinical Performance

### FemoSeal™ Vascular Closure System

|                                        |                                                                                              |
|----------------------------------------|----------------------------------------------------------------------------------------------|
| <b>Manufacturer</b>                    | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 USA          |
| <b>Manufacturer's SRN</b>              | US-MF-000019594                                                                              |
| <b>Management Representative/PRRC</b>  | Kimberly Feitl<br>Vice President, Quality                                                    |
| <b>Basic UDI-DI</b>                    | 38970FS79                                                                                    |
| <b>EMDN number</b>                     | C900199 – Haemostasis Systems-Other                                                          |
| <b>Device Class</b>                    | Class III                                                                                    |
| <b>Year Device was First CE Marked</b> | 2005                                                                                         |
| <b>EU Representative</b>               | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgium<br>SRN: BE-AR-000001433 |
| <b>Notified Body</b>                   | NSAI<br>CE 0050                                                                              |

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This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the FemoSeal™ Vascular Closure System (VCS).

A summary of the safety and clinical performance of the device, intended for users / healthcare professionals, is provided below, in **Section 1.0**.



## **1.0 SUMMARY FOR USERS / HEALTHCARE PROFESSIONALS**

The SSCP is not intended to replace the Instructions for Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients. The SSCP is not intended to replace the mandatory information on the implant cards or in any other mandatory documents.

### **1.1 Intended Use of the Device**

#### **1.1.1 Intended Use**

FemoSeal™ Vascular Closure System is a medical device intended for closure of an arterial puncture after percutaneous catheterization through the common femoral artery.

#### **1.1.2 Indications for Use**

FemoSeal™ Vascular Closure System is indicated for use in closing the common femoral arterial puncture (arteriotomy) in patients who have undergone percutaneous catheterization using a 7F (2.33 mm) or smaller procedural sheath.

#### **1.1.3 Contraindications and/or Limitations**

FemoSeal™ Vascular Closure System is contraindicated in patients with arteriotomies in which sheaths or devices larger than 7F (2.33 mm) have been used.

#### **1.1.4 Target Patient Populations**

The safety and effectiveness of FemoSeal™ Vascular Closure System has been established in patients 18 years of age and older who have undergone percutaneous catheterization using a 7F (2.33 mm) or smaller procedural sheath.

#### **1.1.5 Special Patient Populations**

The safety and effectiveness of FemoSeal™ Vascular Closure System has not been established in the following patient populations:

- Patients with pre-existing autoimmune disease.
- Patients undergoing therapeutic thrombolysis.
- Patients with clinically significant peripheral vascular disease.
- Patients with uncontrolled hypertension (> 220 mmHg systolic or > 110 mmHg diastolic).
- Patients with a bleeding disorder, including thrombocytopenia (< 100,000 platelet count), or anemia (Hgb < 10 mg/dl).
- Patients having an inner lumen of the common femoral artery smaller than 5 mm.

- Patients with renal and/or hepatic impairment.
- Patients with other relevant co-morbidity.
- Population with specific racial and/or ethnic origins.
- Patients with myocardial infarction within 72 hours.
- Patients with a vascular graft or stent at the puncture site.
- Patients who are pregnant or lactating.
- Patients below the age of 18 years.

### **1.1.6 Intended Users**

FemoSeal™ Vascular Closure System's intended users are physicians with training qualifying them to perform arterial access and closure for endovascular procedures through the common femoral artery and have participated in a Terumo Medical Corporation FemoSeal™ physician instruction program.

## **1.2 Device Description**

### **1.2.1 Description of the Device**

FemoSeal™ Vascular Closure System, manufactured by Terumo Medical Corporation (TMC), is a resorbable vascular closure device designed to achieve femoral arterial hemostasis after percutaneous catheterization through the common femoral artery.

FemoSeal™ closure elements consist of two resorbable polymer discs, the inner seal and the outer locking disc, which are held together by a resorbable multifilament, thereby mechanically sealing the arteriotomy (see **Figure 1.1** and **Figure 1.2**). After being deployed through the cone housing sheath, the outer locking disc is tamped onto the multifilament shaft resulting in mechanical closure of the puncture site between the inner and outer locking disc. The inner seal and outer locking disc are held in place via friction on the multifilament shaft. Hemostasis is achieved by mechanical means. The closure elements are degraded by hydrolysis.

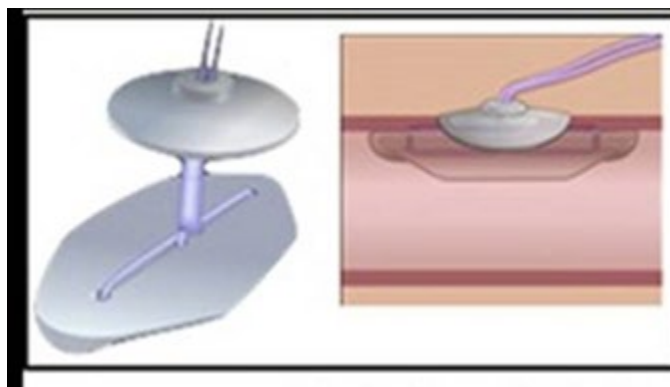
The implantable closure components, inner seal and outer locking disc, are degraded in eighteen (18) months while the multifilament is estimated to be degraded and absorbed via hydrolysis by surrounding tissue after two (2) to three (3) years. The ability of the implantable closure components to maintain compression on the arteriotomy has been tested at up to eight (8) hours. The degradation products are metabolized and excreted in the urine or expired as carbon dioxide via the lungs. No accumulation effects have been observed in animal studies. The additional

components of FemoSeal™ that will come in contact with living tissue or blood during the procedure are the cone housing sheath, dilator, tamping tube, pusher and the guidewire.

**Figure 1.1 Inner Seal and Outer Locking Disc, Respectively**

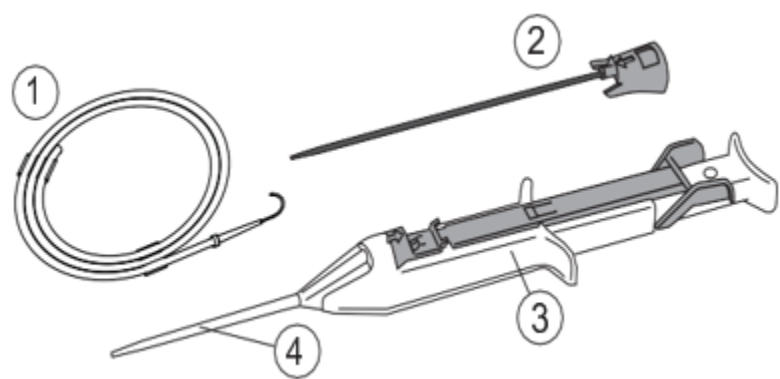


**Figure 1.2 Inner Seal and Outer Locking Disc Deployed**



The FemoSeal™ unit is packaged together with a dilator and a 0.038” (0.97 mm) OD, 27.5” (70 cm) length guidewire and a J-straightener, see **Figure 1.3** below. The guidewire is contained within a polyethylene tube. All parts are packaged in a fixed paper tray. The packaging also includes the patient implant card. The FemoSeal™ Vascular Closure System does not require additional accessories for the device to function as intended and the device is only intended to be used with the dilator and guidewire included within the product’s packaging.

Figure 1.3 FemoSeal™ VCS Unit with the Guidewire and Dilator



1.2.2 Raw Materials & Components

Table 1.1 below list the components of the FemoSeal™ VCS.

Table 1.1 FemoSeal™ VCS Raw Materials and Components

| Part Number | Description                                                |                                                 | Materials                                                                                                                                                                    |
|-------------|------------------------------------------------------------|-------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1           | 0.038" (0.97 mm) Guidewire with a guidewire J-straightener |                                                 | Guidewire: 304 Stainless Steel<br>J-Straightener: Polypropylene, purple pigment<br>Clip: Polyethylene<br>Tubing: Polyethylene                                                |
| 2           | FemoSeal Dilator                                           |                                                 | Hub: Tetrahydrofuran, Blue pigment, Polybutylene terephthalate (PBT)<br><br>Tube: High density polyethylene (HDPE), black pigment<br><br>Lubricant: Silicone Dow Corning 360 |
| 3/4         | FemoSeal Unit                                              | Molded RD7 – Inner Seal and Outer locking Disc* | Copolymer between glycolide, trimethylene carbonate, ε-caprolactone, and TMP: trimethylolpropane (initiator)                                                                 |
|             |                                                            | Multifilament *                                 | Segmented copolymer between L,L-Lactide, trimethylene carbonate, ε-caprolactone, and 1,3 propanediol (initiator)                                                             |

|  |  |                     |                                                                      |
|--|--|---------------------|----------------------------------------------------------------------|
|  |  |                     | Coating is copolymer between glycolide, ε-caprolactone, and L-lysine |
|  |  | Tamping Tube        | Polypropylene                                                        |
|  |  | Pusher              | 304V Stainless steel                                                 |
|  |  | Slider              | Polybutylene terephthalate (PBT)                                     |
|  |  | Housing             | Polybutylene terephthalate (PBT)                                     |
|  |  | Button              | Polybutylene terephthalate (PBT)                                     |
|  |  | Button Lid          | Polyoxymethylene (POM)/Polyacetal Copolymer                          |
|  |  | Sleeve              | Polybutylene terephthalate (PBT)                                     |
|  |  | Spacer              | Polybutylene terephthalate (PBT)                                     |
|  |  | Cone                | Polypropylene                                                        |
|  |  | Housing Lid         | Polybutylene terephthalate (PBT)                                     |
|  |  | Safety Catch        | Polybutylene terephthalate (PBT), blue pigment                       |
|  |  | Sleeve Lid          | Polybutylene terephthalate (PBT)                                     |
|  |  | Tube Gasket         | Silicone shore A 70                                                  |
|  |  | Housing Gasket      | Silicone shore A 50                                                  |
|  |  | Spring              | 302 Stainless Steel                                                  |
|  |  | Cone Housing Sheath | Polypropylene<br>Silicone Dow Corning 360, Hexane                    |

\* Implantable portion of device; implantable components are MRI safe

FemoSeal™ VCS is sterilized via Ethylene Oxide (EO) and is a single-use medical device. The FemoSeal™ VCS device is designed in such a manner that it cannot be re-used.

### **Mode of Action**

The FemoSeal™ VCS promotes mechanical hemostasis by deploying implantable closure elements inside and outside the common femoral artery. The mechanism that prevents bleeding is provided by the inner seal which seals the puncture site, and the outer locking disc which holds the inner seal in position.

### 1.2.3 Clinical Benefit

FemoSeal™ VCS provides the following clinical benefits relative to vascular closure after common femoral arterial puncture:

- Reduction in time to hemostasis<sup>1</sup>
- Reduction in time to ambulation<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

### 1.2.4 Previous Generation(s) or Variants

- The first version of FemoSeal™ VCS (#11200) was sold on the European market during the year 2005 and part of 2006.
- The current FemoSeal™ VCS (#11202), with an improved delivery system, has been on the market since March 28, 2006.

### 1.2.5 Accessories Intended to Be Used in Combination with the Device

The FemoSeal™ unit is packaged together with a dilator, a 0.038” (0.97 mm) OD, 27.5” (70 cm) length guidewire and a J-straightener. The guidewire is an accessory of the FemoSeal™ unit. The J-straightener is a component of the guidewire, while the dilator is a component of the FemoSeal™ unit. The guidewire is the only considered accessory. The guidewire is contained within a polyethylene tube. All parts are packaged in a fixed paper tray. The packaging also includes the patient implant card. The FemoSeal™ Vascular Closure System does not require additional accessories for the device to function as intended and the device is only intended to be used with the dilator and guidewire included within the product’s packaging.

### 1.2.6 Other Devices and Products Intended to Be Used in Combination with the Device

The FemoSeal™ VCS does not require additional devices to function as intended.

## 1.3 Risks and Warnings

### 1.3.1 Residual Risks and Undesirable Effects

Known or foreseeable adverse events, harms and complications associated with the use of the FemoSeal™ VCS as a result of residual risks are listed in **Table 1.2**. Occurrence rate is based on an analysis of the Risk Documentation and calculated based on Post Market Surveillance data from September 1, 2019 through August 31, 2024. There are no unknown residual risks for the FemoSeal™ VCS and all applicable risks have been addressed through the Instructions for Use and risk management process.

Table 1.2. FemoSeal Adverse Events/Complications

| Harm                                 | Occurrence Rate (%) | Mitigating Factors                                                                                                                                                      |
|--------------------------------------|---------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Allergic reaction                    | 0.0000              | Actions and plans to reduce risk as far as possible have been addressed by product design features, manufacturing guidelines, product labeling, and physician training. |
| Aneurysm                             | 0.0000              |                                                                                                                                                                         |
| AV fistula                           | 0.0001              |                                                                                                                                                                         |
| Blood loss / bleeding                | 0.0280              |                                                                                                                                                                         |
| Death                                | 0.0002              |                                                                                                                                                                         |
| Ecchymosis                           | 0.0000              |                                                                                                                                                                         |
| Embolism                             | 0.0000              |                                                                                                                                                                         |
| Foreign body reaction                | 0.0000              |                                                                                                                                                                         |
| Hematoma                             | 0.0027              |                                                                                                                                                                         |
| Hemorrhage                           | 0.0001              |                                                                                                                                                                         |
| Infection                            | 0.0002              |                                                                                                                                                                         |
| Inflammatory reaction                | 0.0000              |                                                                                                                                                                         |
| Numbness                             | 0.0000              |                                                                                                                                                                         |
| Pain                                 | 0.0000              |                                                                                                                                                                         |
| Patient discomfort                   | 0.0004              |                                                                                                                                                                         |
| Procedure delay                      | 0.0065              |                                                                                                                                                                         |
| Pseudoaneurysm                       | 0.0004              |                                                                                                                                                                         |
| Retroperitoneal bleed                | 0.0002              |                                                                                                                                                                         |
| Sepsis                               | 0.0000              |                                                                                                                                                                         |
| Thromboembolism                      | 0.0000              |                                                                                                                                                                         |
| Thrombosis                           | 0.0001              |                                                                                                                                                                         |
| Vessel occlusion/lower limb ischemia | 0.0002              |                                                                                                                                                                         |
| Vessel perforation                   | 0.0000              |                                                                                                                                                                         |
| Vessel tissue dissection/laceration  | 0.0003              |                                                                                                                                                                         |

### 1.3.2 Warnings and Precautions

#### Warnings

1. Do not use if the package has been damaged or any sterile barrier is not intact.
2. Do not use after expiry date – the biodegradable components may not perform adequately.
3. Do not use if any items appear damaged or defective in anyway.
4. Use of FemoSeal™ Vascular Closure System where bacterial contamination of the procedural sheath or the surrounding tissue may have occurred, may cause infection.
5. If it is suspected that the posterior arterial wall has been punctured or more than one arterial puncture has been made, do not rely solely on FemoSeal™ Vascular Closure System to achieve arterial hemostasis. Use additional manual or mechanical compression.
6. If the puncture site is at, or distal to the bifurcation of the femoral artery, FemoSeal™ Vascular Closure System should not be used due to the risk of the Inner Seal being positioned incorrectly. This event may result in bleeding complications and/or disruption to normal blood flow.
7. If there is persistent arterial bleeding from the incision site, do not cut the multifilament until hemostasis is achieved. If hemostasis is not achieved, fasten the multifilament with a sterile wound dressing and apply supplementary compression until hemostasis is achieved. In the case of persistent arterial bleeding, significant bleeding complications may occur which could result in patient injury or death.
8. Do not use the FemoSeal™ Vascular Closure System if the puncture site is proximal to the inguinal ligament as this may result in a retroperitoneal hematoma.
9. Patients at a higher risk for bleeding may suffer increased blood loss, requiring a transfusion.
10. If the inner disc becomes detached it can potentially cause a thrombotic and/or embolic event.

#### Precautions

1. FemoSeal™ Vascular Closure System deployment procedure should be performed by physicians with adequate training in the use of the device.
2. Perform a limited femoral angiogram or an ultrasound-guided femoral puncture prior to FemoSeal™ Vascular Closure System deployment.
3. Discontinue procedure if:
  - Lumen diameter of common femoral artery < 5 mm.



- Stenosis and/or significant plaque present in the vicinity of the common femoral arterial puncture site.
  - Arterial puncture is at, or distal to, the femoral artery bifurcation.
  - Anomalous branches or vessel abnormalities present in the vicinity of the common femoral arterial puncture site.
4. If any hematoma is present, extra care must be taken for correct insertion of the cone housing sheath into the artery.
  5. Use a single wall puncture technique. Do not puncture the posterior wall of the artery.
  6. Observe sterile technique at all times when using FemoSeal™ Vascular Closure System.
  7. FemoSeal™ Vascular Closure System is for single use only and should not be resterilized or reused in any manner. The FemoSeal™ unit is designed in such a manner, that it cannot be re-used.
  8. If deployment of the Inner Seal meets unexpected resistance, discontinue the procedure.
  9. For correct deployment of Inner Seal, reposition your thumb so that the button can spring back freely.
  10. Ensure the tip of the cone housing sheath of FemoSeal™ Unit is under the skin surface before deployment of the Outer Locking Disc. The Outer Locking Disc may inadvertently be deployed above skin level in patients with a short distance between the femoral artery and the skin level.
  11. For correct deployment, a skin incision may be necessary before deployment.
  12. If the Inner Seal is inside the artery, but it is not possible to fully depress the button and deploy the Outer Locking Disc, surgery may be required to remove FemoSeal™ Closure Elements.
  13. If repuncture of the same femoral artery becomes necessary within 18 months, repuncture should be made at least one centimeter proximal to the previous FemoSeal™ Vascular Closure System access site.
  14. Instruct the patient to follow physician's orders regarding closure site inspection.
  15. Instruct the patient to carry the Patient Information Card for the next 18 months

### **Precautions at time of discharge**

Before considering discharge, assess the patient for the following clinical conditions:

1. Bleeding and/or hematoma at the closure site.
2. Pain while walking.

- Signs of infection at the closure site.

### 1.3.3 Field Safety Corrective Actions

There was one Field Safety Corrective Action involving FemoSeal™ VCS during the period from 01 September 2019 through 31 August 2024.

In 2022, Terumo voluntarily recalled FemoSeal™ VCS due to complaints alleging the failures in process and lot release testing of Elkton manufactured FemoSeal product for Tamping Force Measurement and Retraction Force. A total of 950 units were recalled from South Korea.

## 1.4 Clinical Evaluation and Post-Market Clinical Follow-Up

**Table 1.3** includes a list of pivotal studies included to bring FemoSeal™ VCS to market as well as post-market studies and post-market clinical follow up activities. Device version utilized in the study is included in the table below. The first version of FemoSeal™ VCS (#11200) was on the market until 2006, while the next version (#C11202) was released to the market in 2006 and is what is currently in the marketplace today.

**Table 1.3 Summary of Pivotal Studies**

| Pre-Market Functional Animal Testing                                                                                                                                                                                                                                    | Device Version             |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                      |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                      |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                      |
| First In Human Clinical Study                                                                                                                                                                                                                                           |                            |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                      |
| Completed Post-Market Clinical Studies                                                                                                                                                                                                                                  |                            |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                                                                              | C11202<br>(current device) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                                                                                       | C11202<br>(current device) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                                                                                                                                                          | C11202<br>(current device) |

|                                                                                                                                 |                            |
|---------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)          | C11202<br>(current device) |
| <b>Planned / Ongoing Post-Market Clinical Studies</b>                                                                           |                            |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                      | C11202<br>(current device) |
| <b>Post Market Clinical Follow Up Activities</b>                                                                                |                            |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(current device) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(current device) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(current device) |

#### 1.4.1 Summary of Data from Pre-Market (Animal Testing and Clinical Investigations)

Table 1.4 below describes all pre-market studies, both animal testing and clinical investigations.

**Table 1.4 Summaries of Pre-market Studies**

| <b>Pre-Market Functional Animal Testing</b>                                                                                                                                                                                                                             |                                                                      |                                         |                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------|-----------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Name of Study</b>                                                                                                                                                                                                                                                    | <b>Year / CI</b>                                                     | <b>Study Type</b>                       | <b>Objectives</b>                                                                                                                                                                                                                            | <b>Milestones</b>                                                                                                                                                                                                                                                                                                                                        | <b>Potential Acceptance Criteria</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 2000<br>Radi Medical System AB<br><br>Performed by Biomatech, France | Animal study; Exploratory investigation | The aim of the study was to evaluate the biocompatibility and biofunctionality of a biodegradable implant designed to achieve hemostasis in the vascular system. Report addresses reserve animals from Study Number 862 (Document # 1051-01) | N = 3 adult female sheep, 1 animal per time point<br><br>Follow up for histopathologic analysis, macroscopic grading, and ultrastructural analysis<br><br><ul style="list-style-type: none"> <li>12 months</li> <li>15 months</li> <li>18 months</li> </ul><br>Color doppler ultrasound follow up – 30 days at carotid and femoral arterial access sites | Arterial patency <ul style="list-style-type: none"> <li>Post deployment blood flow assessment – 2/3 blood flow reduction associated with temporary arterial vasospasm that was attributed to procedure, both occurred at left common carotid artery</li> <li>Color doppler ultrasound assessment (4 weeks) – 3/3 (100%) without major blood flow reduction 30 days after implantation</li> </ul><br>Macroscopic observations <ul style="list-style-type: none"> <li>12 months – patency confirmed macroscopically by absence of anatomically visible occlusion; no</li> </ul> |

|                                                                                                                 |                             |                                         |                                                                                                          |                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|-----------------------------------------------------------------------------------------------------------------|-----------------------------|-----------------------------------------|----------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                 |                             |                                         |                                                                                                          |                                                                                                                               | <p>macroscopic local intolerance lesions (hemorrhage, necrosis, or neovascularization); encapsulation of internal disc appeared to be marked</p> <ul style="list-style-type: none"> <li>15 months - macroscopic observation showed no signs of inflammation; no residues of inner or outer discs identified; encapsulation tissue located in area of outer disc appeared the same as 12-month observation</li> <li>18 months – macroscopic observation showed no signs of local intolerance, outer disc visible (3/3 cases), degradation of inner disc complete; 1/3 (Left common carotid artery) – depression of artery wall observed at implant site (could be related to device deployment)</li> </ul> <p>Conclusions</p> <ul style="list-style-type: none"> <li>Macroscopically, 12, 15 and 18 months after implantation, no necrotic, degenerative, or thrombotic signs were detected.</li> <li>The degradation process of the inner and outer discs appeared to progress between 12 and 18 months and seemed complete at 18 months, with a whitish tissue covering the implanted area.</li> <li>Histologically, after 18 months, polymer material was no longer visible but an endoluminal fibrous tissue was present. No necrotic, degenerative, or thrombotic lesions were noted.</li> </ul> |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. | 2002 Radi Medical System AB | Animal study; Exploratory investigation | The aim of the study was to evaluate the biocompatibility of a biodegradable implant designed to achieve | Follow up (after implantation) <ul style="list-style-type: none"> <li>12 weeks</li> <li>24 weeks</li> <li>36 weeks</li> </ul> | <u>Patency of carotid and femoral arteries after 4 weeks</u> <ul style="list-style-type: none"> <li>Major blood flow reduction 0/12 (0%)</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |

|                                                                                                                                                         |                                |  |                                    |                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
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| Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | Performed by Biomatech, France |  | hemostasis in the vascular system. | <p>N = 12 sheep, 3 animals per time point, 3 reserve animals sacrificed at 12, 15, and 18 months</p> <p>Implantation sites – right and left femoral arteries, right and left common carotid arteries</p> <p>Color doppler ultrasound analysis</p> | <p><u>No major blood flow reduction</u></p> <ul style="list-style-type: none"> <li>Severe blood flow impairment related to device insertion 0/12 (0%)</li> <li>Blood flow reduction in left common carotid 2/12 (16.6%) due to temporary arterial vasospasm (attributed to surgery, not device)</li> </ul> <p><u>Blood flow impairment by follow up</u></p> <p>12 weeks – 0/12 (0%)<br/> 24 weeks – 0/12 (0%)<br/> 36 weeks – 0/12 (0%)</p> <p>Blood pressure measurements (3 sheep – 36 weeks)</p> <ul style="list-style-type: none"> <li>No major blood flow reduction detected</li> </ul> <p>Macroscopic data for integration and degradation (Grade 0-4)</p> <p><u>Carotid sites</u></p> <p><i>Internal side</i></p> <p>-encapsulation<br/> 12 week 1.3<br/> 24 week 0.8<br/> 36 week 0.7</p> <p>-material degradation<br/> 12 week 2.2<br/> 24 week 2.3<br/> 36 week 0.7</p> <p><i>External side</i></p> <p>-encapsulation<br/> 12 week 2.0<br/> 24 week 1.0<br/> 36 week 0.8</p> <p>-material degradation<br/> 12 week 2.0<br/> 24 week 2.7<br/> 36 week 3.2</p> <p><u>Femoral sites</u></p> <p><i>External side</i></p> <p>-encapsulation<br/> 12 week 1.0<br/> 24 week 2.7</p> |
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|  |  |  |  |  | 36 week 1.0<br>-material degradation<br>12 week 2.0<br>24 week 2.4<br>36 week 3.0<br><br><i>Internal side</i><br>-encapsulation<br>12 week 2.0<br>24 week 1.2<br>36 week 1.0<br>-material degradation<br>12 week 1.0<br>24 week 2.2<br>36 week 3.0<br><br><u>Histological data for integration, degradation, and inflammatory parameters (mean of relevant values, Index 0-4) n=6</u><br><br><u>Carotid sites</u><br>External fibrosis<br>12 weeks – 2.3<br>24 weeks – 2.3<br>36 weeks – 1.8<br>Internal neointima<br>12 weeks – 3.0<br>24 weeks – 2.7<br>36 weeks – 3.3<br>Material degradation<br>12 weeks – 1.7<br>24 weeks – 3.0<br>36 weeks – 3 +<br>Inflammatory parameters (macrophages)<br>12 weeks – 3.0<br>24 weeks – 1.7<br>36 weeks – 1.7<br><u>Femoral sites</u><br>External fibrosis<br>12 weeks – 1.3<br>24 weeks – 1.5<br>36 weeks – 1.7<br>Internal neointima<br>12 weeks – 3.7<br>24 weeks – 3.3<br>36 weeks – 3.8<br>Material degradation<br>12 weeks – 2.0 |
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|                                                                                                                                                 |                                    |              |                                                                                                                                                                           |                                                                                                             | 24 weeks – 3.0<br>36 weeks – 3+<br>Inflammatory parameters (macrophages)<br>12 weeks – 3.5<br>24 weeks – 1.8<br>36 weeks – 1.8<br><br><u>Histomorphological patency values</u><br>Carotid sites<br>12 week 74.0%<br>24 week 81.9%<br>36 weeks -89.43%<br>Femoral sites<br>12 week – 42.2%<br>24 week – 73.21%<br>36 weeks – 78.71%<br><br><u>US vessel patency (mean %)</u><br>Carotid site<br>12 week 94.6%<br>24 week – 96.7%<br>36 week – 94.7%<br>Femoral sites<br>12 week – 66.9%<br>24 week – 63.6%<br>36 week – 75.1%<br><br>Conclusions <ul style="list-style-type: none"> <li>No significant local intolerance sign was detected (absence of visible inflammatory, necrotic, or degenerative lesions) at 12, 24, or 36 weeks</li> <li>No significant adverse tissular reaction recorded with regard to host and device</li> <li>Degradation of implant was nearly complete at 36 weeks</li> </ul> |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in | 2002<br><br>Radi Medical System AB | Animal study | The purpose of the study was to evaluate the biocompatibility and biofunctionality of a biodegradable implant designed to achieve haemostasis in the vascular system. The | Implantation period / follow up is 5 weeks for all animals<br><br>4 sheep, 1 pig<br><br>14 closure elements | Any adverse signs criteria (inflammation, necrosis, hemorrhage, or any other lesion) or any thin pseudo-intimal layer formation were recorded. Particular attention was devoted to initial tissular integration                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |

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| <p>the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>Performed by Biomatech, France</p> | <p>tested device was intended to enter the puncture hole in arteries to achieve haemostasis. One disc entered the puncture hole in the artery and the other tightened the internal disc from outside the artery. Both discs were inserted through an introducer sheath. The discs were designed to prevent bleeding, to heal into the vessel wall and finally degrade and be absorbed. The study was designed to collect and analyze data after functional implantation in the sheep and pig to evaluate the capacity of the implant to maintain physiologic function when used in the circulatory system, to determine the response of the host and the response of the device (physical integrity, tissular encapsulation at sacrifice) and to evaluate the degradation of the implant</p> | <p>8 closure elements implanted in 2 sheep,<br/><br/>2 closure elements implanted in 1 pig<br/><br/>When two closure elements were implanted into same femoral artery, they were implanted at a distance &gt; 30 mm</p> | <p>of the device, with a special emphasis on the internal disc encapsulation.<br/><br/>Macroscopically, no significant signs of local intolerance or thrombus formation were observed. The macroscopic observation did not reveal any difference between the sheep or the pig after implantation of the closure elements in the femoral arteries. Macroscopically, no significant signs of local intolerance or thrombus formation were observed. The macroscopic observation did not reveal any difference between the sheep or the pig after implantation of the closure elements in the femoral arteries.<br/><br/>The histopatological analysis of the implantation site in sheep showed no local adverse reactions. The inner and outer discs showed signs of degradation and were in some cases broken into smaller parts. The inner discs were completely integrated into neointimal tissue. In the pig the histopatological analysis showed slightly more inflammatory signs around the inner and outer discs. In both animals, the multifilament exhibited slightly more inflammatory signs than in the disc material, which is normal for braided sutures</p> |
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|                                                                                                                                                                                                              |                              |                                            |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                         | <p>due to the larger surface area.</p> <p>The vessel patency was measured after 5 weeks using three different methods, histomorphometric, histomorphometric in combination with measurement of vessel diameter by use of caliper and by the use of color doppler ultrasonography. The mean vessel patency in sheep was between 60 and 80 % depending on method (12 observations). In the pig, the mean vessel patency was between 40 and 80 % (2 observations).</p> |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|--------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>First In Human Clinical Study</b>                                                                                                                                                                         |                              |                                            |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| <b>Name of Study</b>                                                                                                                                                                                         | <b>Year / CI</b>             | <b>Study Type</b>                          | <b>Objectives</b>                                                                                                                                                                                                                                                                                                           | <b>Milestones</b>                                                                                                                                                                                                                                                                                                                                       | <b>Potential Acceptance Criteria</b>                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Open label, single arm, multi-centre trial | <p>The objectives of the study were to determine the safety, performance, and effectiveness of the FemoSeal Vascular Closure System (FemoSeal System) in general, and specifically the Closure Elements, in patients undergoing cardiac diagnostic or interventional cardiology procedures using femoral artery access.</p> | <p>2-part study</p> <p>Total n = 80</p> <p>Part 1 n = 20</p> <p>Part 2 n = 60</p> <p>Indications:</p> <p>Part 1 – diagnostic cardiac catheterization using femoral artery as site of access</p> <p>Part 2 – patients undergoing diagnostic and interventional cardiac procedures using femoral artery as the site of access</p> <p>30 day follow up</p> | <p>Outcomes</p> <p><u>hemostasis achieved with FS without compression</u></p> <p>- Part 1 20/20 (100%)</p> <p>- Part 2 58/60 (97%)</p> <p>Median time to hemostasis at time of procedure (part 2) – 1.0 minutes (Range immediate – 8 minutes)</p> <p><u>Time to ambulation (minutes)</u></p> <p>Part 1 –</p> <p>Median: 33.0</p> <p>mean: 67.8</p> <p>Part 2 –</p> <p>median: 45</p> <p>mean: 87.5</p>                                                              |

|  |  |  |  |  | <u>Incidence of major vascular complications – 30 day follow up</u><br>Part 1<br>-Free of vascular complications 20/20 (100%)<br>Part 2<br>Pseudoaneurysm - 1/59 (1.69%)<br><br><u>Treatment failure</u><br>Part 1 – 0/20 (0%)<br>Part 2 – 3/60 (5%) <ul style="list-style-type: none"> <li>2 due to the failure to achieve hemostasis without use of compression</li> <li>1 due to major vascular complication, pseudoaneurysm</li> </ul><br><u>Persistent oozing</u><br>Part 1 – 0/20 (0%)<br>Part 2- 8/60 (13%)<br><br><u>Hematoma</u><br>Part 1 – 0/20 (0%)<br>Part 2 – 6/60 (10%) |
|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

As part of the premarket development plan for FemoSeal™ VCS, 3 animal functional tests were completed. In 2000, prior to initiating clinical studies, an animal study was performed to evaluate the bio-functionality of FemoSeal™ VCS. This study evaluated the capacity of the closure elements to maintain physiologic function and to evaluate their degradation. At 18 months the inner and outer disc material was no longer visible, having been replaced with an endoluminal fibrous tissue. In conclusion, the capacity of the FemoSeal™ VCS closure element to maintain physiologic function when used in the circulatory system was confirmed.

In 2002 an animal study was performed to evaluate the biocompatibility and biofunctionality of a biodegradable implant, FemoSeal™ VCS, designed to achieve hemostasis in the vascular

system. In summary, the degradation of the implant was nearly complete by 36 weeks and there was no significant adverse tissular reaction.

Another animal study in 2002 evaluated the biocompatibility and biofunctionality of a biodegradable implant, FemoSeal™ VCS, designed to achieve hemostasis in the vascular system. After 5 weeks, encapsulation of the disc was complete, and signs of degradation were observed for internal and external discs. In conclusion, the capacity of the implant to maintain physiologic function when used in the circulatory system was confirmed.

As part of the clinical development plan for FemoSeal™ VCS, Radi Medical System AB conducted a pre-market clinical investigation. This clinical investigation is not published or available online. The study with device model #11200 was conducted in 2002-2004 under European Standard EN 540 (Clinical Investigation of Medical Devices for Human Subjects) and in accordance with the ICH General Considerations for Clinical Trials and Guideline for Good Clinical Practice. The details of this study are documented in report EU-SE-001. The clinical trial was documented in the Final Report from Radi Medical Systems AB, “Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures”. The clinical study was performed with FemoSeal™’s first model #11200 and focused on the safety and effectiveness of the implantable closure components. The only difference between the first model #11200 and the current model, C11202, is the French size, 6F and 7F respectively, and the improved delivery system. The clinical benefits, intended use, principles of operation, and the raw materials of the implantable closure elements, inner seal and outer locking disc, remain unchanged.

The intended use of the device was for patients undergoing diagnostic cardiac or interventional cardiac procedures using the femoral artery as an access point. The objective of this study was to determine the safety, performance, and effectiveness of the FemoSeal™ VCS. This was a prospective, multi-center, single arm open-label study with 30-day follow-up.

The primary performance endpoint was time to hemostasis defined as the absence of brisk bleeding. The primary safety endpoint was incidence of major vascular complications through 30-days. Secondary endpoints included time to ambulation, proportion of treatment failures, incidence of adverse events, and device performance characteristics during delivery and deployment.

Patients included in this study were adults able to provide informed consent and with at least one intact pedal pulse. Patients were excluded from the study if they had any of the following conditions:

- History of peripheral vascular disease
- Autoimmune disease
- Known bleeding disorder or severe anemia

- INR >1.5
- Myocardial infarct with 72 hours
- Uncontrolled hypertension despite treatment
- Obesity precluding access with Seldinger technique
- Presence of vascular graft or stent at arteriotomy site
- Previous ipsilateral puncture within 3 months
- Life expectancy < 6 months

Additionally, patients were examined intraoperatively and excluded from the study if any of the following were observed:

- Lumen diameter of common femoral artery <5mm
- Arterial branches within 2 cm proximal to puncture site
- Significant stenosis within 3 cm of puncture site
- Use of primary introducer sheath >6Fr
- Puncture at or distal to femoral bifurcation
- Multiple femoral punctures
- Known or suspected posterior femoral wall puncture
- Large hematoma (2:6 cm) at completion of the procedure
- Difficult primary sheath insertion for procedure due to tortuous tissue or vessel

This single protocol study was conducted in two parts: 20 patients were enrolled during Part 1, then a safety analysis was completed, and then an additional 60 patients were enrolled during Part 2.

In Part 1, mean age of enrolled patients was 65.9 years, 70.0% of patients were male, and 95% of patients were on concomitant medications. In Part 2 of the study, mean age was 63.8 years, 78% were male, and 100% were on concomitant medications.

Patients undergoing diagnostic (Part 1 and Part 2) or interventional (Part 2) cardiac catheterization procedures were eligible for enrollment in the study. The procedures were compliant with standard of care at each of the enrolling hospitals, followed by use of the FemoSeal™ VCS. Patient data was collected at baseline, during the procedure, and at 1-day and 30-days post-procedure. Results are summarized in **Table 1.5** and indicate FemoSeal™ VCS is safe and effective for use in this patient population.

**Table 1.5 Clinical Results Reported in Pre-Market Study**

|                                                                                                   | Part 1       | Part 2                    |
|---------------------------------------------------------------------------------------------------|--------------|---------------------------|
| Number of patients                                                                                | 20           | 60                        |
| Mean Time to Hemostasis                                                                           | 1.2 minutes  | 1.6 minutes <sup>a</sup>  |
| Mean Time to Ambulation                                                                           | 72.2 minutes | 87.5 minutes <sup>b</sup> |
| Incidence of Major Vascular Complications <sup>c</sup>                                            | 0 (0%)       | 1 (2%)                    |
| Number of Patients with Adverse Events                                                            | 5 (25%)      | 19 (32%)                  |
| Treatment failure (defined as major vascular complications, need for manual compression, or both) | 0 (0%)       | 3 (5%)                    |
| Device Malfunctions                                                                               | 0 (0%)       | 6 (10%)                   |

<sup>a</sup>Based on total sample size of 58 because 2 patients did not reach hemostasis at time of procedure due to previous ipsilateral punctures. Hemostasis was achieved at 7 minutes and 37 minutes for these patients.

<sup>b</sup>Based on total sample size of 59: 1 patient was not included because they were placed on ventilator due to pulmonary edema and unable to ambulate for over a week.

<sup>c</sup>Defined as vascular complication requiring blood transfusion or surgical repair, or local infection requiring administration of antibiotic, hospitalization or extension of hospitalization, or site debridement

No major vascular complications were observed in Part 1 of the study. There was 1 major vascular complication reported in Part 2 of the study: pseudoaneurysm that was reported within 1 day post-procedure. The event required ultrasound guided compression and an injection of thrombin into the pseudoaneurysm, and extended the patient's hospitalization.

Of the 5 adverse events reported in Part 1 of the study, there was 1 possibly device-related adverse event: a non-serious event of brisk bleeding at 1-day post procedure. Of the 19 adverse events reported in Part 2 of the study, 3 device-related non-serious adverse events of hematoma were observed, and 6 possibly device-related non-serious events were observed including 3 reports of persistent oozing, 2 hematomas, and 1 leg pain after exercise.

There were 3 patients in Part 2 considered treatment failures: 2 due to failure to achieve hemostasis without the use of compression and 1 due to the major vascular complication (pseudoaneurysm). There were no treatment failures in Part 1 of the study.

Of the six device malfunctions in Part 2 of the study, three did not interfere with the procedure, one was attributed to user error, one was leakage of the introducer, and one was a broken filament joint. The last two issues were addressed with model updates implemented in C11202.

Part 2 of the pre-market clinical study did not report the 6-month follow-up results due to patient non-compliance. The pre-market clinical study (EU-SE-001) 30-day results, which is in line with the clinical literature's follow-up time period, demonstrates that FemoSeal™ VCS is safe and effective.

## 1.4.2 Summary of Data from Post-Market Clinical Studies

There were 4 completed post-market clinical studies described in **Table 1.6** below. These clinical investigations are not published or available online.

**Table 1.6 Post-Market Clinical Studies**

| Completed Post-Market Clinical Studies                                                      |                                                           |                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                  |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
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| Name of Study                                                                               | Year / CI                                                 | Study Type                                             | Objectives                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Milestones                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Potential Acceptance Criteria                                                                                                    |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br><br>RADI                                          | Post Market Study, User Acceptability of New Packaging | Post-market study carried out on the model update FemoSeal Vascular® Closure System #11202 which has a modified delivery system compared to the first model, #11200, to document functionality.<br><br>The objective of the study was to get feedback on the revised Instructions for Use (IFU), the training project for physicians and nurse, to confirm the assessments made in the risk analysis and to give input to any product quality improvements. | 100 patients <ul style="list-style-type: none"><li>63 male / 37 females</li><li>Mean age 68 years for female, 65 years for males</li></ul> 2 Swedish hospitals, 6 physicians<br><br>112 devices<br><br>Data captured on patient record forms (CRF)<br><br>Planned observation time – 30 minutes from time of application                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Outcomes<br><br>1. Illustrations/Instructions in IFU considered informative and adequate<br><br>2. Immediate hemostasis (91/100) |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)           | Dr. Nicolas Moes<br>Innsbruck Medical University, Austria | Post - Market Confirmatory Assessment                  | The objective of this study was to assess safety and performance of FemoSeal® used during normal clinical routine in patients undergoing diagnostic cardiac catheterization or percutaneous cardiac interventional procedure performed with 7F-sheath.                                                                                                                                                                                                      | 50 consecutive patients<br><br>Indication – diagnostic or invasive cardiac catheterization from common femoral artery<br><br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systemic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.8</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systemic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.8 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Primary endpoints <ul style="list-style-type: none"><li>Primary efficacy endpoint – TTH (time to hemostasis) with or without oozing but without any additional compression, manual or mechanical.</li><li>Safety endpoint - incidence of adverse events - minor and major vascular complications and all other adverse events – serious and non-serious during duration of the study (i.e., until patient discharge).</li></ul><br>Outcomes <ul style="list-style-type: none"><li>Mean time to hemostasis</li></ul> |
| n                                                                                           | 50                                                        |                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                  |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| men                                                                                         | 35 (70%)                                                  |                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                  |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| women                                                                                       | 15 (30%)                                                  |                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                  |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| PCI cases                                                                                   | 15                                                        |                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                  |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| age (yrs)                                                                                   | 62.8±11.1                                                 |                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                  |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| body mass index (kg/m²)                                                                     | 25.4±6.7                                                  |                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                  |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| systemic BP (mmHg)                                                                          | 131.2±20.9                                                |                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                  |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| diastolic BP (mmHg)                                                                         | 77.9±10.8                                                 |                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                  |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| diabetes mellitus                                                                           | 9 (18%)                                                   |                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                  |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| arterial hypertension                                                                       | 34 (68%)                                                  |                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                  |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| previous coronary intervention                                                              | 13 (26%)                                                  |                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                  |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| preprocedure aspirin                                                                        | 50 (100%)                                                 |                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                  |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| preprocedure clopidogrel                                                                    | 50 (100%)                                                 |                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                  |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Procedural unfractionated heparin                                                           | 15 (30%)                                                  |                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                  |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Procedural abciximab                                                                        | 2 (4%)                                                    |                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                  |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |

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|                                                                                                                                 |                                 |                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                | <ul style="list-style-type: none"> <li>Diagnostic - <math>56.6 \pm 29</math> seconds</li> <li>Interventional <math>59.9 \pm 16.2</math> seconds</li> <li>All patients <math>57.8 \pm 26.3</math></li> <li>All patients could be ambulated after 4 hours bed rest without any problems.</li> </ul> <p>Safety outcomes</p> <ul style="list-style-type: none"> <li>49/50 (98%) free of vascular complications until hospital discharge</li> <li>Mean time to discharge 2.6 days</li> <li>1/50 (2%) minor bleeding next day after uneventful ambulation on day of angiography</li> </ul> |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | 2009 RADI                       | Post Market Study                                     | <p>The study should inform if the customers/users perceived any problems with the new package, especially the non-sterile outer side of the Tuvek/PET-PE pouch.</p> <p>The study should also give information about if the treating physician perceives any differences in the application/deployment steps of the device compared to previously used devices.</p> <p>The study should also give input to any further needs for product quality improvement.</p> | <p>25 devices</p> <p>4 Swedish hospitals</p> <p>16/25 (64%) of patients were PCI patients with heavy anti-coagulation medications</p>                                                                                                                                                                                          | <p>Outcomes</p> <ol style="list-style-type: none"> <li>Package related problems – 21/25 (84%) applications were successful; 4/25 (16%) were unsuccessful (1 - testing new introducer, 1 inner disc when through arteriotomy at backing step, button came up and outer disc was placed in incision tissue canal, 2 immediate hemostasis was not achieved despite no deployment issues.)</li> <li>Immediate hemostasis 19/25 (76%) patients</li> <li>Bleeding 11/25 (44%) – 9/25 (36%) oozing/bleeding, 2/25 (8%) hematomas</li> </ol> <p>Total event rate 19%</p>                     |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022) | 2022/Terumo Medical Corporation | Prospective, Multi-center, Observational, Post-market | To further demonstrate the safety and effectiveness of the FemoSeal™ VCS in achieving hemostasis of common femoral artery (CFA) access site in real-world subjects undergoing percutaneous endovascular procedures                                                                                                                                                                                                                                               | <ul style="list-style-type: none"> <li>Patient follow-up at 30 days (<math>\pm 7</math> days) by hospital visit or telephone call.</li> <li>Enrollment: December 2021 through July 2022.</li> <li>230 enrolled subjects undergoing diagnostic or interventional endovascular procedures in which FemoSeal™ is used.</li> </ul> | <ul style="list-style-type: none"> <li><b>Demographics/comorbidities:</b> <ul style="list-style-type: none"> <li>- Gender: 161 males (70 %)/69 females 69 (30%).</li> <li>- Mean age: <math>70 \pm 12</math>.</li> <li>- BMI: <math>26.1 \pm 4.95</math> kg/m<sup>2</sup>.</li> <li>- Hypertension: 160 patients (69.6 %).</li> <li>- Dyslipidemia: 128 (55.7 %).</li> </ul> </li> </ul>                                                                                                                                                                                             |

|  |  |  |  |                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|--|--|--|--|-----------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  | <p>3 European sites: France (92 patients), Germany (38 patients), Belgium (100 patients).</p> | <ul style="list-style-type: none"> <li>- Coronary artery disease: 42 (18.3%).</li> <li>- Current smoker: 86 (37.6 %).</li> <li>- Past smoker: 66 (28.8%).</li> <li>- Coronary heart disease: 34 (14%).</li> <li>- Previous myocardial infarction: 18 (7.8%).</li> <li>- Peripheral artery revascularization: 12 (5.2 %) carotid and 83 (37.5%) and low limb artery.</li> <li>- Antiplatelet therapy (at baseline): 211 (91,7 %), including 21 (9.1%) dual antiplatelet therapy (DAPT).</li> <li>- Oral anticoagulation: 40 (17.4%) patients.</li> <li>• <b>Intervention characteristics:</b> <ul style="list-style-type: none"> <li>- Setting: inpatient clinic 162 cases (70.4%), outpatient clinic 68 cases (29.6%).</li> <li>- Prevailing indication: claudication 147 cases (63.9%).</li> <li>- Approach: 35 antegrade (15.3%), 194 retrograde (84.7%).</li> </ul> </li> <li>• <b>Primary Endpoints:</b> <ul style="list-style-type: none"> <li>- Combined safety (freedom from major complications of the access site limb within 6 hours post-procedure) and effectiveness (successful puncture site hemostasis) endpoint achieved in 215/226 (95.1%) [95% CI: 91.46; 97.55] patients in the Full Analysis Set and 215/230 (93.5%) [95% CI 89.47, 96.30] in the FemoSeal™ Treated Set.</li> <li>- Effectiveness endpoint was achieved in 219/226</li> </ul> </li> </ul> |
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|  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  | <p>(96.9%) CI [93.7, 98.7] of patients.</p> <p>- Safety endpoint achieved in 220/230 (95.2%) [95% CI: 92.15, 97.90] patients.</p> <p>• <b>Secondary endpoints:</b></p> <p>- Freedom from minor access site complications for six hours post-procedure achieved in 225/230 (97.8%) [95% CI: 95.00; 99.29].</p> <p>- Freedom from major and minor access site complications from six hours to 30 days post-procedure achieved in 219/230 (95.2%) [95% CI:91.60; 97.59] of patients.</p> <p>- Median Time to hemostasis with FemoSeal™ VCD: 0.42 (0.25; 0.50) minutes.</p> <p>- Median Time to ambulation: 5.00 (4.54; 5.50) minutes.</p> <p>- Median length of stay in hospital: 23.98 (22.72, 25.00) hours.</p> <p>- FemoSeal™ VCS usability: ‘easy’ or ‘very easy’ to deploy in 98.7% of cases (‘easy’ to deploy in 21 (9.2%), ‘very easy’ to deploy in 205 (89.5 %)) with no or low resistance at deployment in 226 (98.3%) of cases.</p> <p>152/230 (66.1%) of patients treated using guidewire included with the FemoSeal™ kit (GW 0.038”) and recommended in the FemoSeal™ without any reported device deficiencies or adverse events.</p> |
|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

The 2006 study was conducted to confirm the safety and effectiveness of the current device with an improved delivery system and to get feedback on the FemoSeal™ VCS IFU and training program. The study included 100 patients and the primary endpoint was whether hemostasis was achieved, or if additional manual or mechanical compressions was needed. This study concluded that the application of FemoSeal™ VCS was successful in the majority of cases (91% achieved immediate hemostasis).

The 2008 study enrolled 50 patients to assess the safety and performance of FemoSeal™ VCS when used during normal clinical routine in patients undergoing cardiac catheterization with a 7 Fr sheath. The primary endpoint for the study was to collect data on the time to hemostasis and the time to ambulation without additional compression, manual or mechanical. The study results concluded that the mean time to hemostasis was 57.8 seconds and all patients ambulated after 4 hours of bed rest.

The 2009 study was to evaluate the new FemoSeal™ VCS packaging. 25 patients were enrolled in the study. The primary endpoint was whether the user experienced any problems with the packaging. The users noted no problems regarding the new FemoSeal™ VCS packaging. This study also collected data for the time to hemostasis.

The 2022 study was to proactively collect safety and effectiveness data of FemoSeal VCS in achieving hemostasis of common femoral artery (CFA) access site in real-world subjects undergoing percutaneous endovascular procedures. 230 patients were enrolled in the study. The primary endpoints for the registry are procedural success (i.e., successful puncture site hemostasis) and reduction in major complications (e.g., vascular injury, access site-related bleeding, access site infection, repeat manual compression, and new access site-related ipsilateral acute leg ischemia). The study concluded that the FemoSeal™ VCS performs well in real-world settings and provides effective haemostasis and low rates of access-site complications for patients undergoing peripheral endovascular interventions. It demonstrates a good performance with short time to haemostasis and good operator usability feedback, which makes FemoSeal™ VCS a valuable device for femoral access closure.

### 1.4.3 Summary of Data from Post-Market Clinical Follow-Up

#### 1.4.3.1 Completed Post-Market Clinical Follow-Up

A summary of the completed post-market clinical follow-up activities is described in **Table 1.7** below.

**Table 1.7. Post-Market Clinical Follow-Up Activities**

| Completed Post-Market Clinical Follow-Up Activities |         |            |            |            |                               |
|-----------------------------------------------------|---------|------------|------------|------------|-------------------------------|
| Name of Activity                                    | Year/CI | Study Type | Objectives | Milestones | Potential Acceptance Criteria |

| Completed Post-Market Clinical Follow-Up Activities                        |          |                                                   |                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|----------------------------------------------------------------------------|----------|---------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021 ) | 2021 TMC | Post Market Clinical Survey – high quality survey | Post-market survey to collect prospective feedback related to the use of the FemoSeal™ Vascular Closure Device distributed in the European Union markets.                                                                        | <ul style="list-style-type: none"> <li>120 cases</li> <li>8 unique physicians with &gt; 5 years experiences</li> <li>Multiple countries in Europe</li> </ul>                                                                                                                                                                                                                                                 | <b>1-5 Scale device evaluations – Survey statements</b> <ul style="list-style-type: none"> <li>Acceptance criteria <ul style="list-style-type: none"> <li>Ratings 3-5 are deemed favorable</li> <li>All statements should have ≥ 80% positive feedback</li> </ul> </li> <li>Outcomes <ul style="list-style-type: none"> <li>No survey statement received &gt; 20% unfavorable responses</li> <li>No complaints against product were filled</li> </ul> </li> </ul> |
| 20210298 – 0.035” and 0038” Guidewire Clinical Survey Report (2021 )       | 2021 TMC | Post Market Clinical Survey – high quality survey | Post-market survey to collect prospective feedback related to the use of the 0.035” guidewire included with 6Fr Angio-Seal™ VIP Vascular Closure Device (VCD) and 0.038” included with both 8Fr Angio-Seal™ VIP VCD and FemoSeal | <ul style="list-style-type: none"> <li>Surveys for 0.035” wire <ul style="list-style-type: none"> <li>106 surveys <ul style="list-style-type: none"> <li>64 physicians</li> </ul> </li> </ul> </li> <li>Surveys for 0.038” wire <ul style="list-style-type: none"> <li>109 surveys <ul style="list-style-type: none"> <li>55 physicians</li> </ul> </li> </ul> </li> <li>12 retrospective surveys</li> </ul> | <b>1-5 Scale device evaluations – Survey statements</b> <ul style="list-style-type: none"> <li>Acceptance criteria <ul style="list-style-type: none"> <li>Ratings 3-5 are deemed favorable</li> <li>All statements should have ≥ 80% positive feedback</li> </ul> </li> <li>Outcomes <ul style="list-style-type: none"> <li>All guidewires received acceptable ratings</li> <li>No complaints against</li> </ul> </li> </ul>                                      |

| Completed Post-Market Clinical Follow-Up Activities                                                                             |                     |                                                   |                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|---------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                 |                     |                                                   | Vascular Closure System distributed in the European Union markets.                                              |                                                                                                                                                                                                                                                                                                                                                                                 | product were filed                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024<br>TMC/TE | Post Market Clinical Survey – high quality survey | To prospectively collect feedback related to the use FemoSeal VCS with guidewires distributed in the EU market. | <ul style="list-style-type: none"> <li>126 Surveys               <ul style="list-style-type: none"> <li>7 sites</li> <li>5 countries</li> </ul> </li> <li>14 November 2023-11 June 2024</li> <li>Physician medical specialty:               <ul style="list-style-type: none"> <li>Vascular surgery</li> <li>Interventional radiology</li> <li>Angiology</li> </ul> </li> </ul> | <b>5 Scale device evaluations – Survey statements</b> <ul style="list-style-type: none"> <li>Acceptance criteria               <ul style="list-style-type: none"> <li>Ratings 3-5 are deemed favorable</li> <li>All statements should have ≥ 80% positive feedback</li> <li>If adverse events occur in this survey, they should be those anticipated by the risk management</li> </ul> </li> <li>Patient Demographics               <ul style="list-style-type: none"> <li>Female: 29.4% (37/126)</li> <li>Male: 69.8% (88/126)</li> <li>Sex not disclosed: 0.8 (1/126)</li> <li>Age &gt;75 years: 31.7%</li> </ul> </li> <li>Outcomes               <ul style="list-style-type: none"> <li>Guidewire supplied with the FemoSeal™ VCS:</li> </ul> </li> </ul> |

| Completed Post-Market Clinical Follow-Up Activities |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-----------------------------------------------------|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                     |  |  |  |  | 101/126<br>(80.2%).<br><ul style="list-style-type: none"> <li>○ Procedure duration (minutes): 63.4 (36.6) (mean (SD)); 57.0 (36.0-81.0) (Median (IQR))</li> <li>○ All FemoSeal™ VCS performance ratings were favorable.</li> <li>○ All FemoSeal™ VCS-supplied guidewire ratings were favorable.</li> <li>○ One (0.8%) adverse event: the FemoSeal™ VCS discs were not well aligned probably because of the use of a stiff guidewire (Boston Scientific Amplatz Super Stiff, 75 cm, 0.035 inch) requiring manual compression to achieve hemostasis.</li> </ul> |

| Completed Post-Market Clinical Follow-Up Activities |  |  |  |  |  |
|-----------------------------------------------------|--|--|--|--|--|
|                                                     |  |  |  |  |  |

Terumo Medical Corporation has completed three high-quality physician user surveys during the current reporting period (01 September 2019-31 August 2024).

The FemoSeal™ Clinical Surveys collected proactive clinical data in relation to the safety and performance of the FemoSeal™ VCS during clinical use. The survey included questions focused on the overall device and associated accessories including the 0.038” guidewire, and their direct interactions. The Guidewire clinical surveys collected proactive clinical data in relation to safety and performance during clinical use of the 0.038” guidewire supplied with FemoSeal™ VCS. The survey questions focused specifically on the general use of the guidewire ranging from insertion through the procedural sheath into the vasculature through removal of the wire.

The FemoSeal™ VCS and 0.038” guidewire included with the device received all acceptable ratings and six (6) complaints were filed for the device and nine (9) non-complaints for the guidewire based on evaluation of the comments received from the high-quality clinical surveys. The complaints have been evaluated for both the FemoSeal and the guidewire and were assessed as part of Terumo post-market surveillance process. There were no new risks and or risk levels identified.

A physician user survey was completed in 2024 as part of PMCF activities. The results of the survey demonstrated that the FemoSeal™ VCS performance rating and safety were overall very favorable. The compatibility of other guidewires than the one standard provided with the FemoSeal™ VCS was also demonstrated.

**1.4.3.2 Ongoing/Planned Post-Market Clinical Follow-Up**

TMC has one ongoing/planned post-market clinical follow-up activities. A clinical survey will be completed to prospectively collect feedback related to the use of the guidewire with FemoSeal VCS distributed in the EU market. The survey will be completed by physicians to study which guidewires they used during the procedure. The purpose of this survey is to address a gap identified as the lack of literature and external reviewer commentary on the FemoSeal™ VCS compatibility with the use of other guidewires from non-Terumo brands. The feedback includes technical outcomes, clinical performance, and safety pertaining to the performance of the device with different guidewires.

**1.4.4 Summary of Data from Systematic Literature Review**

Terumo Medical Corporation conducts systematic literature reviews to collect and evaluate clinical safety and performance data from published studies on the FemoSeal™ VCS and/or

similar devices. The aim of the annual screening of the published literature is to identify previously unknown side-effects, monitor known side effects, identify emergent risks, and identify possible systematic misuse or off-label use of the FemoSeal™ VCS.

The most recent systematic literature review, which covered the period from September 1, 2019 through August 31, 2024, identified 29 published studies that provided clinical safety and performance data on the FemoSeal™ VCS. Twenty-three references reported on-label usage of FemoSeal™ VCS and off-label usage was reported in nine studies. Overall, the literature review of studies specific to the use of FemoSeal™ VCS shows a population under study that is representative of patients in the EU undergoing percutaneous vascular catheterization procedures. See **Section 3** for a list of these 23 on-label peer-reviewed publications.

Clinical performance was assessed by the following measures:

- Time to hemostasis is better than or comparable to the State of the Art for percutaneous common femoral artery closure.
- Time to ambulation is better than or comparable to the State of the Art for percutaneous closure of the common femoral artery.
- Rate of post-operative complications are comparable or lower than the current standards of care.

Based on these clinical performance measures, the data in this literature review showed that FemoSeal™ VCS can be used successfully in closing the femoral arterial puncture (arteriotomy) in patients who have undergone percutaneous catheterization using a 7 Fr or smaller procedural sheath. Complete hemostasis was achieved in a majority of patients (79.65-100%) of the cases and was associated with a median time to hemostasis of 0.5min, mean time to discharge of 3 days. Between 69.2-86.7% of patients were able to ambulate 5 hr after closure, with a mean post-operative bedrest of 349 min. FemoSeal™ VCS failure was observed in 3.68-4% of cases, and additional manual compression was needed in 0.9-4.4% of procedures.

Clinical safety was assessed by adverse events including, but not limited to:

- Bleeding
- Hematoma
- Pseudoaneurysm
- Bruise
- Arteriovenous Fistula
- Infection
- Death

For each of these adverse events, the rate of occurrence reported for FemoSeal™ VCS in the included studies was less than or comparable to historically reported rates for manual compression and other vascular closure devices.

No adverse events were identified through review of 10 case reports, as no new, unanticipated, emerging, or unacceptable risks were identified.

The overall effectiveness of using FemoSeal™ VCS during diagnostic angiography or interventional operations depends on multiple factors such as: gender, age, patient anatomy, comorbidities, anatomical placement of the puncture site, surgeon's experience, VCD deployment method, postoperative care, etc. In addition to technical success including achievement of hemostasis, FemoSeal™ VCS offered clinical benefits relative to vascular closure after femoral arterial puncture such as reduction in time to hemostasis, reduction in time to ambulation. The performance outcomes for the FemoSeal™ VCS are consistent with those expected for this type of device when used as intended. Some of the references retrieved during the current search period showed the use of the subject device in an anatomical location other than the common femoral artery and for closure of arteriotomies > 7 Fr, which is considered off-label.

No unknown side-effects, emergent risks, or possible systematic misuse of the device were identified during review. However, if the FemoSeal™ VCS is used with care by trained physicians the medical device performs as a useful and necessary clinical device. Overall, the target therapy and therefore the FemoSeal™ VCS address the clinical need that currently exists in treatment of vascular access related complications.

Overall, the data in this literature review did not identify any performance or safety issues in the clinical setting that were previously unknown, or adverse effects that occurred at higher than anticipated / acceptable rates. Therefore, it can be concluded from this literature review that FemoSeal™ VCS, when used to provide compression for hemostasis at the arteriotomy following percutaneous catheterization, continues to perform as expected and is not associated with serious safety events.

#### **1.4.5 Summary of Data from Post-Market Surveillance**

A proactive PMS system is in place and a review of all complaints is completed on a monthly basis and in compliance with internal manufacturing procedures. Complaint data was analyzed during the time period of September 1, 2019 to August 31, 2024. Overall, there were 28 Medical Device Vigilance (MDV) Reports and 476 customer complaint reports submitted to the manufacturer. Of the 28 MDV reports, 27 were related to adverse events and one to device malfunction. There were two deaths during the reporting period, but none of the reported deaths were adjudicated to be related to the subject device. Among the 476 complaints made to the manufacturer, the most common reasons for complaints was deployment difficulties (146 occurrences, 0.0142% occurrence rate). Failure mode of pullout events is the second most occurring with a rate of 0.0126% (130 events).



FemoSeal™ Vascular Closure System has over 1,030,136 sales globally and 827,843 in the European Economic Area. The calculated frequency of complaints based on global sales is 0.046%. The overall customer complaint rate is very low. No new risks were identified that are not included in the IFU and risk documentation.

The occurrence rates for the undesirable side effects are shown in **Table 1.2**. No new unanticipated, emerging, or unacceptable risks were identified through the complaints. There were no significant increases in the frequency or severity of known undesirable side effects.

#### **1.4.6 Overall Summary of Clinical Performance and Safety**

FemoSeal™ VCS is indicated for use in closing the common femoral arterial puncture (arteriotomy) in patients who have undergone percutaneous catheterization using a 7F (2.33 mm) or smaller procedural sheath. This clinical evaluation is based on a comprehensive analysis of available pre- and post-market clinical data and literature relevant to the intended use of the FemoSeal™ VCS.

A comprehensive review of the published literature was conducted covering the period from September 1, 2019, through August 31, 2024. The body of evidence included 29 studies for the FemoSeal™ VCS. The evidence provided in the clinical evaluation concludes that when used as indicated, the subject device is safe and effective and any risks or undesirable side effects, which may be associated with the device under normal conditions of use, constitute acceptable risks when weighed against the benefits to the patient. The performance outcomes for the subject devices are consistent with those expected for this type of device when used as intended.

The potential undesirable side-effects associated with the use of FemoSeal™ VCS include the adverse events commonly reported with alternative means of arteriotomy closure, e.g., bleeding and hematoma. Overall, the occurrence rates for the adverse events reported with the use of FemoSeal™ VCS are similar to the rates reported with manual compression and similar vascular closure devices. Specifically, for bleeding and hematoma, the reported rates for FemoSeal™ VCS are less than the reported rates for similar vascular closure devices. Each of the reported adverse events, from both the published literature and post-market surveillance, had been previously identified (see **Section 1.3**).

The existing data regarding the clinical safety and performance of suggest that patient benefits from use of this vascular closure device outweigh possible risks when it is used in accordance with the Instruction for Use.

As indicated in the previous sections above, the data provided for FemoSeal™ VCS demonstrates the consistency between the data related to the device under evaluation (e.g., device usage, safety outcomes, clinical performance, and clinical benefits), identified equivalent devices and the data related to similar devices listed in the State of the Art.

The cross-analysis of safety data did not identify any gaps between the following:

- Data mentioned in the State of the Art
- Data specific to the device under evaluation
- Data mentioned in the Risk Management File(s)
- Data mentioned in the labelling and/or IFU (i.e., residual risks to be conveyed to the user are addressed).

Clinical safety has been demonstrated by low rates of complications identified in the published per-reviewed clinical literature, company sponsored clinical studies, review of the post-market data coupled with no market withdrawals. No concerns with performance have been identified, the literature reviewed contained use of FemoSeal™ VCS that was consistent with the manufacturer's intended use.

### **1.5 Possible Diagnostic or Therapeutic Alternatives**

Manual compression is traditionally used to achieve hemostasis at the arteriotomy site after vascular catheterizations. Manual compression has been associated with the patient being immobilized for long periods of time (up to 8 hours after a procedure) and with substantial discomfort and extended hospital stays. A recent systematic review found that the median time to achieve hemostasis with manual compression was 20.8 minutes.<sup>1</sup>

Alternatives to manual compression include external hemostatic devices that apply mechanical compression to the arteriotomy site. These devices do not shorten the time to hemostasis or time to ambulation but reduce the personnel requirements by replacing manual compression with mechanical compression. Adverse event rates associated with the use of mechanical compression are similar to rates with manual compression.

Vascular closure devices, such as FemoSeal™ VCS, are designed to close the arteriotomy. They aim to reduce the time to hemostasis and enable earlier ambulation. A recent systematic review, including 13 commercially available devices, found that the median time to achieve hemostasis with a vascular closure device was 5.4 minutes. The median hemostasis time for the individual vascular closure devices ranged from 1 minute (FemoSeal™ VCS) to 14 minutes; with the majority of devices being between 4 and 10 minutes.<sup>1</sup>

Commonly reported adverse events associated with closure of the arteriotomy site, with manual compressions, external hemostatic devices, or vascular closure devices, include hematoma, bleeding at the access site, pseudoaneurysm, arteriovenous fistula, and infection. The same systematic review (34 randomized controlled trials, 14,401 patients) found that the rates of adverse events were similar between manual compression and the use of vascular closure devices, with the exception that bleeding tended to be a little higher with vascular closure devices.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Suggested User Profile and Training

FemoSeal™ Vascular Closure System’s intended users are physicians with training qualifying them to perform arterial access and closure for endovascular procedures through the common femoral artery and have participated in a Terumo Medical Corporation FemoSeal™ physician instruction program.

## 1.7 Relevant Harmonized and Common Standards

| Standard Reference | Current Year of Compliance/Rev | Description                                                                                                                              |
|--------------------|--------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070          | 2014/AMD1:2018                 | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070       | 2014/A1:2018                   | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance       | May 20, 2021                   | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052         | 2015                           | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213         | 2017                           | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503         | 2020                           | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182         | 2019                           | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |
| EN ISO 13485       | 2016/A11:2021                  | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |

| Standard Reference | Current Year of Compliance/Rev | Description                                                                                                                                                              |
|--------------------|--------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 13485          | 2016                           | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 14644-1        | 2015                           | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1     | 2015                           | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2        | 2015                           | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2     | 2015                           | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3        | 2019                           | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3     | 2019                           | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1        | 2003                           | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1     | 2003                           | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2        | 2003/TC1:2004                  | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| EN ISO 14698-2     | 2003/TC 1:2004                 | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |

| Standard Reference     | Current Year of Compliance/Rev | Description                                                                                                          |
|------------------------|--------------------------------|----------------------------------------------------------------------------------------------------------------------|
| USP <788>              | N/A                            | PARTICULATE MATTER IN INJECTIONS                                                                                     |
| EU Pharmacopeia 2.9.19 | N/A                            | Particulate Contamination: Sub-Visible Particles                                                                     |
| IEC 62366-1            | 2015                           | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN 62366-1             | 2015                           | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN ISO 14971           | 2019/A11:2021                  | Medical devices — Application of risk management to Medical devices                                                  |
| ISO 14971              | 2019                           | Medical devices — Application of risk management to Medical devices                                                  |
| ASTM F1980             | 2016                           | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1         | 2020                           | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1            | 2018                           | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2         | 2006                           | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2            | 2006                           | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3         | 2014                           | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3            | 2014                           | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4         | 2017                           | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |

| Standard Reference | Current Year of Compliance/Rev | Description                                                                                                    |
|--------------------|--------------------------------|----------------------------------------------------------------------------------------------------------------|
| ISO 10993-4        | 2017                           | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood               |
| EN ISO 10993-5     | 2009                           | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                             |
| ISO 10993-5        | 2009                           | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                             |
| EN ISO 10993-6     | 2016                           | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                  |
| ISO 10993-6        | 2016                           | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                  |
| EN ISO 10993-10    | 2023                           | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                 |
| ISO 10993-10       | 2021                           | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                 |
| EN ISO 10993-11    | 2018                           | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                |
| ISO 10993-11       | 2017                           | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                |
| EN ISO 10993-12    | 2021                           | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                 |
| ISO 10993-12       | 2021                           | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                 |
| EN ISO 10993-17    | 2009                           | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances |
| ISO 10993-17       | 2002                           | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances |

| Standard Reference | Current Year of Compliance/Rev | Description                                                                                                                                                                  |
|--------------------|--------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-18       | 2020/A1:2022                   | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-18    | 2020/A1:2022                   | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-23    | 2021                           | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23       | 2021                           | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382         | 2018                           | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756          | 2017                           | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>           | N/A                            | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>          | N/A                            | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72     | 2019                           | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135       | 2014/A1:2019                   | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135          | 2014/A1:2018                   | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |

| Standard Reference | Current Year of Compliance/Rev | Description                                                                                                                                                     |
|--------------------|--------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-7     | 2008/A1:2022                   | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                       |
| ISO 10993-7        | 2008/A1:2019                   | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                               |
| EN 556-1           | 2024                           | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices |
| EN ISO 11737-1     | 2018/A1:2021                   | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11737-1        | 2018/A1:2021                   | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| EN ISO 11138-1     | 2017                           | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-1        | 2017                           | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| EN ISO 11138-2     | 2017                           | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 11138-2        | 2017                           | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| EN ISO 15223-1     | 2016                           | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| ISO 15223-1        | 2016                           | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| EN 1041            | 2008/A1:2013                   | Information supplied by the manufacturer of medical devices                                                                                                     |



| Standard Reference | Current Year of Compliance/Rev | Description                                                                                                                                                                |
|--------------------|--------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 11607-1     | 2020/A1:2023                   | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| ISO 11607-1        | 2019/A1:2023                   | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| EN ISO 11607-2     | 2020/A1:2023                   | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ISO 11607-2        | 2019/A1:2023                   | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169         | 2016                           | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M  | 2016                           | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825         | 2018                           | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096         | 2011 (R 2019)                  | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M      | 2015                           | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24       | 2021                           | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3        | 2020                           | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |
| MDCG 2020-8        | 2020                           | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                             |

| Standard Reference | Current Year of Compliance/Rev | Description                                                                                                                                                                                                                                                   |
|--------------------|--------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-7        | 2020                           | Post-market clinical follow-up (PMCF) Plan Template<br>A guide for manufacturers and notified bodies                                                                                                                                                          |
| MDCG 2020-6        | 2020                           | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                                                                                                          |
| MDCG 2019-9 v1     | 2022                           | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                                                                                      |
| MDCG 2019-8 v2     | 2020                           | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15       | 2020                           | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11       | 2021                           | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19       | 2021                           | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4     | 2021                           | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2        | 2019                           | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1        | 2019                           | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7        | 2018                           | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6        | 2018                           | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device                                                                                                                                                                |

| Standard Reference  | Current Year of Compliance/Rev | Description                                                                                                                                                                                   |
|---------------------|--------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                     |                                | Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                                                  |
| MDCG 2018-4         | 2018                           | MDCG 2018-4 Annex: UDI database<br>Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                               |
| MDCG 2018-3 v1      | 2020                           | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25        | 2021                           | Regulation (EU) 2017/745 - application of MDR requirements to ‘legacy devices’ and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2.12-2 Rev 2 | 2012                           | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                        |

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### 3.0 REVISION HISTORY

| SSCP revision number      | Date issued      | Change description                                                         | Revision validated by the Notified Body                                                                                                                                                                                                                                                                   |
|---------------------------|------------------|----------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022              | January 20, 2023 | Initial Issue, upon MDR CE certification                                   | <input checked="" type="checkbox"/> Yes<br>Validation language: English<br><input type="checkbox"/> No (only applicable for class IIa or some IIb implantable devices (MDR, Article 52 (4) 2nd paragraph) for which the SSCP is not yet validated by the NB)<br><input type="checkbox"/> Other (explain): |
| SSCP-FS-2023 – Revision 1 | March 15, 2024   | Updated for the period between January 1, 2019 through December 31, 2023.  | <input checked="" type="checkbox"/> Yes<br>Validation language: English<br><input type="checkbox"/> No (only applicable for class IIa or some IIb implantable devices (MDR, Article 52 (4) 2nd paragraph) for which the SSCP is not yet validated by the NB)<br><input type="checkbox"/> Other (explain): |
| SSCP-FS-2024 Revision 1   |                  | Updated for the period between September 1, 2019, through August 31, 2024. | <input type="checkbox"/> Yes<br>Validation language: English<br><input type="checkbox"/> No (only applicable for class IIa or some IIb implantable devices (MDR, Article 52 (4) 2nd paragraph) for which the SSCP is not yet validated by the NB)<br><input type="checkbox"/> Other (explain):            |
| SSCP-FS-2024 Revision 2   | June 20, 2025    | Revised based on NSAI queries for validation                               | <input checked="" type="checkbox"/> Yes<br>Validation language: English                                                                                                                                                                                                                                   |

|  |  |  |                                                                                                                                                                                                                                                   |
|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  | <div><input type="checkbox"/> No (only applicable for class IIa or some IIb implantable devices (MDR, Article 52 (4) 2nd paragraph) for which the SSCP is not yet validated by the NB)</div> <div><input type="checkbox"/> Other (explain):</div> |
|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|



**Обобщение на безопасността и клиничното представяне****FemoSeal™ Vascular Closure System**

|                                                       |                                                                                             |
|-------------------------------------------------------|---------------------------------------------------------------------------------------------|
| <b>Производител</b>                                   | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 САЩ         |
| <b>SRN на производителя</b>                           | US-MF-000019594                                                                             |
| <b>Представител на<br/>ръководството/PRRC</b>         | Кимбърли Фейтл<br>Vice President по качеството                                              |
| <b>Базов UDI-DI</b>                                   | 38970FS79                                                                                   |
| <b>EMDN номер</b>                                     | C900199 - Системи за хемостаза-други                                                        |
| <b>Клас на изделието</b>                              | Клас III                                                                                    |
| <b>Година на първа CE<br/>маркировка на изделието</b> | 2005                                                                                        |
| <b>Представител в ЕС</b>                              | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Белгия<br>SRN: BE-AR-000001433 |
| <b>Нотифициран орган</b>                              | NSAI<br>CE 0050                                                                             |

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Настоящото обобщение на безопасността и клиничната ефикасност (SSCP) е предназначено да предостави публичен достъп до актуализирано обобщение на основните аспекти на безопасността и клиничното действие на FemoSeal™ Vascular Closure System (VCS).

Обобщение на безопасността и клиничната ефикасност на изделието, предназначено за потребители / медицински специалисти, е предоставено в **раздел 1.0**.

## **1.0 ОБОБЩЕНИЕ ЗА ПОТРЕБИТЕЛИ/МЕДИЦИНСКИ СПЕЦИАЛИСТИ**

SSCP не е предназначено да замени инструкциите за употреба като основен документ, за да се гарантира безопасната употреба на изделието, нито е предназначено да предоставя диагностични или терапевтични предложения на предвидените потребители или пациенти. SSCP не е предназначено да замени задължителната информация на картите за импланти или в други задължителни документи.

### **1.1 Предназначение на изделието**

#### **1.1.1 Предназначение**

FemoSeal™ Vascular Closure System е медицинско изделие, предназначено за затваряне на артериална пункция след перкутанна катетеризация през общата феморална артерия.

#### **1.1.2 Показания за употреба**

FemoSeal™ Vascular Closure System е предназначена за затваряне на пункция на общата феморална артерия (артериотомия) при пациенти, които са били подложени на перкутанна катетеризация с помощта на 7F (2,33 mm) или по-малък процедурен катетър.

#### **1.1.3 Противопоказания и/или ограничения**

FemoSeal™ Vascular Closure System е противопоказана при пациенти с артериотомия, при която са използвани катетри или изделия с размер по-голям от 7F (2,33 mm).

#### **1.1.4 Целеви популации пациенти**

Безопасността и ефективността на FemoSeal™ Vascular Closure System са установени при пациенти на възраст над 18 години, които са били подложени на перкутанна катетеризация с помощта на 7F (2,33 mm) или по-малък процедурен катетър.

#### **1.1.5 Специални популации пациенти**

Безопасността и ефективността на FemoSeal™ Vascular Closure System не са установени в следните популации пациенти:

- Пациенти с предварително съществуващо автоимунно заболяване.
- Пациенти, подложени на терапевтична тромболиза.
- Пациенти с клинично значимо периферно съдово заболяване.
- Пациенти с неконтролирана хипертония (> 220 mmHg систолно или > 110 mmHg диастолно).

- Пациенти с нарушение на кръвосъсирването, включително тромбоцитопения ( $< 100\,000$  брой на тромбоцити) или анемия ( $Hgb < 10\text{ mg/dl}$ ).
- Пациенти с вътрешен лумен на общата феморална артерия по-малък от 5 mm.
- Пациенти с бъбречно и/или чернодробно увреждане.
- Пациенти с други свързани съпътстващи заболявания.
- Пациенти със специфичен расов и/или етнически произход.
- Пациенти, прекарвали миокарден инфаркт през последните 72 часа.
- Пациенти със съдов графт или стент на мястото на пункцията.
- Пациентки, които са бременни или кърмят.
- Пациенти на възраст под 18 години.

#### 1.1.6 Целеви потребители

Целевите потребители на FemoSeal™ Vascular Closure System са лекари с обучение, което ги квалифицира да извършват артериален достъп и затваряне след ендоваскуларни процедури през общата феморална артерия и които са участвали в програма за обучение на лекари на Terumo Medical Corporation за FemoSeal™.

### 1.2 Описание на изделието

#### 1.2.1 Описание на изделието

FemoSeal™ Vascular Closure System, произведена от Terumo Medical Corporation (TMC), е резорбируемо устройство за затваряне на съдове, предназначено за постигане на хемостаза на феморалната артерия след перкутанна катетеризация през общата феморална артерия.

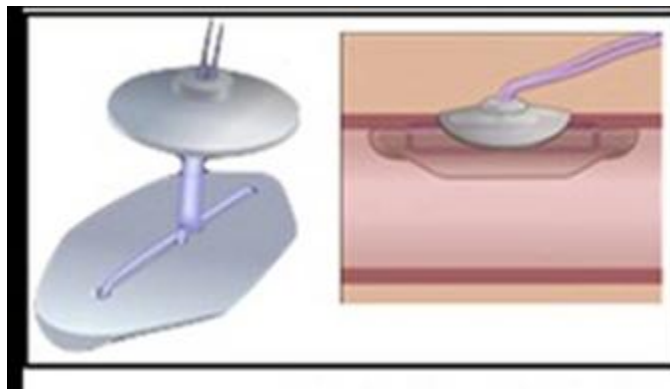
Затварящите елементи на FemoSeal™ представляват два резорбируеми полимерни диска, вътрешно уплътнение и външен заключващ диск, които са прикрепени един към друг чрез резорбируем мултифиламент, като по този начин механично запечатват артериотомията (вижте **Фигура 1.1** и **Фигура 1.2**). След като бъде поставен през конуса, съдържащ катетър, външният заключващ диск се притиска върху мултифиламентния сноп, което води до механично затваряне на мястото на пункцията между вътрешния и външния заключващ диск. Вътрешното уплътнение и външният заключващ диск се придържат чрез триене върху мултифиламентния сноп. Хемостаза се постига по механичен път. Затварящите елементи се разграждат чрез хидролиза.

Имплантируемите компоненти за затваряне, вътрешното уплътнение и външният заключващ диск се разграждат за осемнадесет (18) месеца, докато мултифиламентът се счита за разграден и абсорбиран чрез хидролиза от околната тъкан след две (2) до три (3) години. Способността на имплантируемите компоненти за затваряне на съдове да поддържат компресията върху артериотомията е тествана до осем (8) часа. Продуктите на разграждане се метаболизират и екскретират в урината или се извеждат като въглероден диоксид през белите дробове. При проучвания върху животни не са наблюдавани ефекти на натрупване. Допълнителните компоненти на FemoSeal™, които ще влязат в контакт с жива тъкан или кръв по време на процедурата, са конусът, съдържащ катетър, дилататорът, работната тръба, тласкачът и водачът.

**Фигура 1.1 Вътрешно уплътнение и външен заключващ диск, съответно**

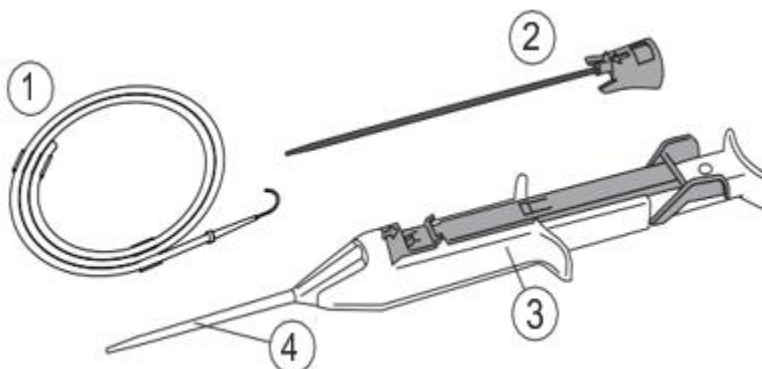


**Фигура 1.2 Вътрешно уплътнение и външен заключващ диск, поставени**



Изделието FemoSeal™ е опаковано заедно с дилататор и водач с 0,038" (0,97 mm) OD, 27,5" (70 cm) дължина и J-изправител, вижте **Фигура 1.3** по-долу. Водачът се намира в полиетиленова тръба. Всички части са опаковани във фиксирана хартиена тава. Опаковката включва и картата на импланта на пациента. FemoSeal™ Vascular Closure System не изисква допълнителни аксесоари, за да може изделието да функционира по предназначение, като изделието е предназначено да се използва само с дилататора и водача, включени в опаковката на продукта.

**Фигура 1.3 FemoSeal™ VCS с водач и дилататор**



## 1.2.2 Суровини и компоненти

**Таблица 1.1** по-долу изброява компонентите на FemoSeal™ VCS.

**Таблица 1.1** Суровини и компоненти на FemoSeal™ VCS

| Номер на частта | Описание                                        |                                                             | Материали                                                                                                                                                                              |
|-----------------|-------------------------------------------------|-------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1               | 0,038" (0,97 mm) водач с J-изправител на водача |                                                             | Водач: Неръждаема стомана 304<br>J-изправител: Полипропилен, бял пигмент<br>Скоба: Полиетилен<br>Тръби: Полиетилен                                                                     |
| 2               | Дилататор FemoSeal                              |                                                             | Главина: Тетрахидрофуран, син пигмент, полибутилен терефталат (PBT)<br><br>Тръба: Полиетилен с висока плътност (HDPE), черен пигмент<br><br>Лубрикант: Силикон Dow Corning 360, хексан |
| 3/4             | FemoSeal елемент                                | Формован RD7 – вътрешно уплътнение и външен заключващ диск* | Съполимер между гликолид, триметилен карбонат, ε-капролактон и TMP: триметилпропан (инициатор)                                                                                         |
|                 |                                                 | Мултифиламент *                                             | Сегментиран съполимер между L,L-лактид, триметилен карбонат, ε-капролактон и 1,3 пропандиол (инициатор)<br><br>Покритието е съполимер между гликолид, ε-капролактон и L-лизин          |
|                 |                                                 | Работна тръба                                               | Полипропилен                                                                                                                                                                           |



|  |  |                         |                                                 |
|--|--|-------------------------|-------------------------------------------------|
|  |  | Тласкач                 | Неръждаема стомана 304                          |
|  |  | Плъзгач                 | Полибутилен терефталат (PBT)                    |
|  |  | Корпус                  | Полибутилен терефталат (PBT)                    |
|  |  | Бутон                   | Полибутилен терефталат (PBT)                    |
|  |  | Капак на бутона         | Полиоксиметилен (POM)/полиацетален кополимер    |
|  |  | Втулка                  | Полибутилен терефталат (PBT)                    |
|  |  | Разделител              | Полибутилен терефталат (PBT)                    |
|  |  | Конус                   | Полипропилен                                    |
|  |  | Капак на корпуса        | Полибутилен терефталат (PBT)                    |
|  |  | Предпазител             | Полибутилен терефталат (PBT), син пигмент       |
|  |  | Капак на втулката       | Полибутилен терефталат (PBT)                    |
|  |  | Уплътнение на тръбата   | Силиконов ръб А 70                              |
|  |  | Уплътнение на корпуса   | Силиконов ръб А 50                              |
|  |  | Пружина                 | Неръждаема стомана 302                          |
|  |  | Конус, съдържащ катетър | Полипропилен<br>Силикон Dow Corning 360, хексан |

\* Имплантируема част на изделието; имплантируемите компоненти са безопасни за ЯМР

FemoSeal™ VCS е стерилизирана с етиленов оксид (EO) и е медицинско изделие за еднократна употреба. Изделието FemoSeal™ VCS е проектирано по такъв начин, че да не може да се използва повторно.

### **Начин на действие**

FemoSeal™ VCS насърчава механичната хемостаза чрез разполагане на имплантируеми затварящи елементи от вътрешната и външната страна на феморалната артерия. Механизмът, който предотвратява кървенето, се осигурява от вътрешното уплътнение, което затваря мястото на пункцията, и външния заключващ диск, който държи вътрешното уплътнение фиксирано.

### **1.2.3 Клинична полза**

FemoSeal™ VCS осигурява следните клинични ползи по отношение на съдовото затваряне след пункция на общата феморална артерия:

- Намаляване на времето до хемостаза<sup>1</sup>

- Намаляване на времето до раздвижване<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

#### 1.2.4 Предходно(и) поколение(я) или варианти

- Първата версия на FemoSeal™ VCS (№11200) се продаваше на европейския пазар през 2005 г. и част от 2006 г.
- Настоящата FemoSeal™ VCS (№11202), с подобрена система за доставяне, е на пазара от 28 март 2006 г.

#### 1.2.5 Аксесоари, предназначени за използване в комбинация с устройството

Системата FemoSeal™ е опакована заедно с дилататор и водач с 0,038” (0,97 mm) OD 27,5” (70 cm) дължина и J-изправител. Водачът е аксесоар за системата FemoSeal™. J-изправителят е компонент на водача, докато дилататорът е компонент на системата FemoSeal™. Водачът е единственият специален аксесоар. Водачът се намира в полиетиленова тръба. Всички части са опаковани във фиксирана хартиена тава. Опаковката включва и картата на импланта на пациента. FemoSeal™ Vascular Closure System не изисква допълнителни аксесоари, за да може изделието да функционира по предназначение, като изделието е предназначено да се използва само с дилататора и водача, включени в опаковката на продукта.

#### 1.2.6 Други изделия и продукти, предназначени за използване в комбинация с изделието

FemoSeal™ VCS не изисква допълнителни изделия, за да функционира по предназначение.

### 1.3 Рискове и предупреждения

#### 1.3.1 Остатъчни рискове и нежелани ефекти

Известни или предвидими нежелани събития, вреди и усложнения, свързани с употребата на устройството FemoSeal™ VCS в резултат на остатъчни рискове, са изброени в **Таблица 1.2**. Честотата се основава на анализ на документацията за риска и се изчислява въз основа на данни от наблюдение след пускане на пазара от 1 септември 2019 г. до 31 август 2024 г. Няма неизвестни остатъчни рискове за FemoSeal™ VCS и всички приложими рискове са разгледани чрез Инструкциите за употреба и процеса на управление на риска.

**Таблица 1.2. Нежелани събития/усложнения, свързани с FemoSeal**

| Вреди                                   | Честота (%) | Смекчаващи фактори                                                                                                                                                                                            |
|-----------------------------------------|-------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Алергична реакция                       | 0,0000      | Действията и планове за намаляване на риска до възможно най-ниско ниво са заложи в характеристиките на дизайна на продукта, указанията за производството и етиктирането на продукта и обучението на лекарите. |
| Аневризма                               | 0,0000      |                                                                                                                                                                                                               |
| Артериовенозна фистула                  | 0,0001      |                                                                                                                                                                                                               |
| Загуба на кръв/крвоизлив                | 0,0280      |                                                                                                                                                                                                               |
| Смърт                                   | 0,0002      |                                                                                                                                                                                                               |
| Екхимоза                                | 0,0000      |                                                                                                                                                                                                               |
| Емболия                                 | 0,0000      |                                                                                                                                                                                                               |
| Реакция на чуждо тяло                   | 0,0000      |                                                                                                                                                                                                               |
| Хематом                                 | 0,0027      |                                                                                                                                                                                                               |
| Хеморагия                               | 0,0001      |                                                                                                                                                                                                               |
| Инфекция                                | 0,0002      |                                                                                                                                                                                                               |
| Възпалителна реакция                    | 0,0000      |                                                                                                                                                                                                               |
| Изтръпване                              | 0,0000      |                                                                                                                                                                                                               |
| Болка                                   | 0,0000      |                                                                                                                                                                                                               |
| Дискомфорт на пациента                  | 0,0004      |                                                                                                                                                                                                               |
| Отлагане на процедурата                 | 0,0065      |                                                                                                                                                                                                               |
| Псевдоаневризма                         | 0,0004      |                                                                                                                                                                                                               |
| Ретроперитонеален крвоизлив             | 0,0002      |                                                                                                                                                                                                               |
| Сепсис                                  | 0,0000      |                                                                                                                                                                                                               |
| Тромбоемболия                           | 0,0000      |                                                                                                                                                                                                               |
| Тромбоза                                | 0,0001      |                                                                                                                                                                                                               |
| Съдова оклузия/исхемия на долен крайник | 0,0002      |                                                                                                                                                                                                               |
| Перфорация на съд                       | 0,0000      |                                                                                                                                                                                                               |
| Дисекция/разкъсване на съдова тъкан     | 0,0003      |                                                                                                                                                                                                               |

### 1.3.2 Предупреждения и предпазни мерки

#### Предупреждения

1. Не използвайте, ако опаковката е повредена или някоя стерилна бариера е нарушена.
2. Не използвайте след изтичане на срока на годност – биоразградимите компоненти може да не работят адекватно.
3. Не използвайте, ако някои елементи изглеждат повредени или дефектни.
4. Използването на FemoSeal™ Vascular Closure System на място, където може да е настъпило бактериално замърсяване на катетъра или на околната тъкан, може да причини инфекция.
5. Ако има съмнения, че задната артериална стена е пробита или е направена повече от една артериална пункция, не разчитайте единствено на FemoSeal™ Vascular Closure System за постигане на артериална хемостаза. Използвайте допълнителна ръчна или механична компресия.
6. Ако мястото на пункцията е върху или дистално от бифуркацията на феморалната артерия, FemoSeal™ Vascular Closure System не трябва да се използва поради риска от неправилно позициониране на вътрешното уплътнение. Това събитие може да доведе до усложнения, свързани с кръвоизлив и/или нарушаване на нормалния кръвен поток.
7. Ако има персистиращо артериално кървене от мястото на разреза, не режете мултифиламента, докато не се постигне хемостаза. Ако не се постигне хемостаза, затегнете мултифиламента със стерилна превръзка и приложете допълнителна компресия, докато се постигне хемостаза. В случай на персистиращ артериален кръвоизлив може да настъпят значителни усложнения, свързани с кръвоизлива, които могат да доведат до нараняване или смърт на пациента.
8. Не използвайте FemoSeal™ Vascular Closure System, ако мястото на пункцията е проксимално на ингвиналния лигамент, тъй като това може да доведе до ретроперитонеален хематом.
9. Пациентите с по-висок риск от кръвоизлив може да претърпят повишена загуба на кръв, изискваща кръвопреливане.
10. Ако вътрешният диск се откачи, това може потенциално да причини тромботично и/или емболично събитие.

## Предпазни мерки

1. Процедурата по поставяне на FemoSeal™ Vascular Closure System трябва да се извършва от лекари с подходящо обучение за използване на изделието.
2. Направете ограничена феморална ангиограма или феморална пункция под ултразвук преди поставянето на FemoSeal™ Vascular Closure System.
3. Прекратете процедурата, ако:
  - Диаметърът на лумена на общата феморална артерия е  $< 5$  mm.
  - Има стеноза и/или значителна плака в близост до мястото на пункцията на общата феморална артерия.
  - Артериалната пункция е върху или дистално от бифуркацията на феморалната артерия.
  - Има аномални разклонения или аномалии на съдове в близост до мястото на пункцията на общата феморална артерия.
4. Ако има някакъв хематом, трябва да се положат допълнителни грижи за правилното поставяне на конуса, съдържащ катетър, в артерията.
5. Използвайте техника за пробиване на една стена. Не пробивайте задната стена на артерията.
6. Спазвайте стерилна техника през цялото време, когато използвате FemoSeal™ Vascular Closure System.
7. FemoSeal™ Vascular Closure System е само за еднократна употреба и не трябва повторно да се стерилизира или да се използва повторно по никакъв начин. Изделието FemoSeal™ е проектирано по такъв начин, че да не може да се използва повторно.
8. Ако при поставянето на вътрешното уплътнение срещнете неочаквано съпротивление, прекратете процедурата.
9. За правилно поставяне на вътрешното уплътнение поставете палеца си така, че бутонът да може да се върне свободно назад.
10. Уверете се, че върхът на конуса, съдържащ катетър, на изделието FemoSeal™ е под повърхността на кожата, преди да поставите външния заключващ диск. Външният заключващ диск може по невнимание да се постави над нивото на кожата при пациенти с малко разстояние между феморалната артерия и нивото на кожата.
11. За правилно поставяне може да е необходим разрез на кожата преди поставянето.

12. Ако вътрешното уплътнение е вътре в артерията, но не е възможно да натиснете докрай бутона и да се постави външния заключващ диск, може да се наложи операция за отстраняване на затварящите елементи на FemoSeal™.
13. Ако се наложи повторната пункция на същата феморална артерия в рамките на 18 месеца, повторната пункция трябва да се извърши най-малко на един сантиметър проксимално от предишното място за достъп на FemoSeal™ Vascular Closure System.
14. Инструктирайте пациента да следва инструкциите на лекаря относно инспекцията на мястото на затваряне.
15. Инструктирайте пациента да носи картата с информация за пациента през следващите 18 месеца

### **Предпазни мерки при изписване**

Преди да обмислите изписване, направете оценка на пациента за следните клинични състояния:

1. Кръвоизлив и/или хематом на мястото на затваряне.
2. Болка при ходене.
3. Признаци на инфекция на мястото на затваряне.

### **1.3.3 Коригиращи действия за безопасност на терен**

Имаше едно коригиращо действие за безопасност на терен, включващо FemoSeal™ VCS, за периода от 01 септември 2019 г. до 31 август 2024г.

През 2022 г. Terumo доброволно изтегли FemoSeal VCS поради оплаквания, в които се твърди за неуспехи в тестването на процеса и освобождаването на партидата на произведения от Elkton продукт FemoSeal за измерване на силата на запресоване и силата на ретракция. Общо 950 единици бяха изтеглени от Южна Корея.

## **1.4 Клинична оценка и клиничното проследяване след пускане на пазара**

**Таблица 1.3** включва списък на основни проучвания, проведени за пускане на FemoSeal™ VCS на пазара, както и постмаркетингови проучвания и постмаркетингови клинични дейности по проследяване. Версията на изделието, използвана в проучването, е включена в таблицата по-долу. Първата версия на FemoSeal™ VCS (№11200) беше на пазара до 2006 г., докато следващата версия (№C11202) беше пусната на пазара през 2006 г. и е това, което в момента се предлага на пазара.

**Таблица 1.3 Резюме на основните проучвания**

| <b>Функционално тестване върху животни преди пускане на пазара</b>                                                                                                                                                                                                      | <b>Версия на изделието</b>     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                          |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                          |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                          |
| <b>Първо клинично проучване при хора</b>                                                                                                                                                                                                                                |                                |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                          |
| <b>Завършени клинични проучвания след пускане на пазара</b>                                                                                                                                                                                                             |                                |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                                                                              | C11202<br>(настоящото изделие) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                                                                                       | C11202<br>(настоящото изделие) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                                                                                                                                                          | C11202<br>(настоящото изделие) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)                                                                                                                                                  | C11202<br>(настоящото изделие) |
| <b>Планирани/текущи постмаркетингови клинични проучвания</b>                                                                                                                                                                                                            |                                |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                                                                                                                                                              | C11202<br>(настоящото изделие) |
| <b>Постмаркетингови дейности за клинично проследяване</b>                                                                                                                                                                                                               |                                |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                                                                                                                                                               | C11202<br>(настоящото изделие) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                                                                                                                                                                      | C11202<br>(настоящото изделие) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024)                                                                                                                                         | C11202<br>(настоящото изделие) |

### 1.4.1 Резюме на данните от предпазарни проучвания върху животни и клинични изследвания

**Таблица 1.4** по-долу описва всички предпазарни проучвания, както върху животни, така и клинични.

**Таблица 1.4 Резюме на предпазарните проучвания**

| Функционално тестване върху животни преди пускане на пазара                                                                                                                                                                                                             |                                                                          |                                                  |                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Име на проучването                                                                                                                                                                                                                                                      | Година/CI                                                                | Тип на проучването                               | Цели                                                                                                                                                                                                                                                 | Основни етапи                                                                                                                                                                                                                                                                                                              | Потенциални критерии за приемане                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 2000<br><br>Radi Medical System AB<br><br>Изпълнен от Biomatech, Франция | Проучване върху животни; проучвателно изследване | Целта на проучването беше да се оцени биосъвместимостта и биофункционалността на биоразградим имплант, предназначен за постигане на хемостаза в съдовата система. Докладът се отнася до резервни животни от проучване номер 862 (документ № 1051-01) | Бр. = 3 възрастни женски овце, 1 животно на времева точка<br><br>Проследяване за хистопатологичен анализ, макроскопско класифициране и ултраструктурен анализ<br><br>• 12 месеца<br>• 15 месеца<br>• 18 месеца<br><br>Ехографско проследяване с цветен Доплер – 30 дни на места на каротиден и феморален артериален достъп | Артериална проходимост<br>• Оценка на кръвния поток след поставяне – 2/3 намаление на кръвния поток, свързано с временен артериален вазоспазъм, който се приписва на процедурата, и двата се появиха в лявата обща каротидна артерия<br>• Преглед с ехограф с цветен Доплер (4 седмици) – 3/3 (100%) без значително намаляване на кръвния поток 30 дни след имплантирането<br><br>Макроскопски наблюдения<br>• 12 месеца – макроскопски потвърдена проходимост чрез липса на анатомично видима оклузия; липса на макроскопски лезии на локална непоносимост (хеморагия, некроза или неоваскуларизация); капсулирането на вътрешния диск изглеждаше ясно<br>• 15 месеца - макроскопското наблюдение не показва признаци на възпаление; не са открити остатъци от вътрешни или външни дискове; капсулираната тъкан, разположена в областта на външния диск, изглеждаше същата, като при 12-месечното наблюдение<br>• 18 месеца – макроскопското наблюдение не показва |



|                                                                                                                                                                                                                                                                                |                                                                          |                                                         |                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|---------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                                                                                                |                                                                          |                                                         |                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                           | <p>признаци на локална непоносимост, видим външен диск (3/3 случая), пълно разграждане на вътрешния диск; 1/3 (лява обща каротидна артерия) – депресия на стената на артерията, наблюдавано на мястото на имплантиране (може да е свързано с поставянето на устройството)</p> <p>Заклучения</p> <ul style="list-style-type: none"> <li>Макроскопски, 12, 15 и 18 месеца след имплантирането, не са открити некротични, дегенеративни или тромботични признаци.</li> <li>Процесът на разграждане на вътрешните и външните дискове изглежда напредва между 12 и 18 месеца и завършва към 18-я месец, с белезникава тъкан, покриваща имплантираната област.</li> <li>Хистологично, след 18 месеца, полимерният материал вече не се вижда, но има наличие на ендолуминална фиброза тъкан. Не са отбелязани некротични, дегенеративни или тромботични лезии.</li> </ul> |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002 Radi Medical System AB</p> <p>Изпълнен от Biomatech, Франция</p> | <p>Проучване върху животни; проучвателно изследване</p> | <p>Целта на проучването беше да се оцени биосъвместимостта на биоразградим имплант, предназначен за постигане на хемостаза в съдовата система.</p> | <p>Проследяване (след имплантиране)</p> <ul style="list-style-type: none"> <li>12 седмици</li> <li>24 седмици</li> <li>36 седмици</li> </ul> <p>Бр. = 12 овце, 3 животни на времева точка, 3 резервни животни, умъртвени в 12-я, 15-я и 18-я месец</p> <p>Места на имплантиране – дясна и лява феморална артерия, дясна и лява обща каротидна артерия</p> | <p><u>Проходимост на каротидните и феморалните артерии след 4 седмици</u></p> <ul style="list-style-type: none"> <li>Значително намаляване на кръвния поток 0/12 (0%)</li> </ul> <p><u>Няма значително намаляване на кръвния поток</u></p> <ul style="list-style-type: none"> <li>Тежко нарушение на кръвния поток, свързано с поставянето на изделията 0/12 (0%)</li> <li>Намаляване на кръвния поток в лявата обща каротидна артерия 2/12 (16,6%) поради временен артериален вазоспазм (приписан</li> </ul>                                                                                                                                                                                                                                                                                                                                                      |

|  |  |  |  | Цветен доплеров ултразвуков анализ | <p>на операцията, не на изделието)</p> <p><u>Нарушение на кръвния поток при проследяване</u></p> <p>12 седмици – 0/12 (0%)</p> <p>24 седмици – 0/12 (0%)</p> <p>36 седмици – 0/12 (0%)</p> <p>Измерване на кръвното налягане (3 овце – 36 седмици)</p> <ul style="list-style-type: none"> <li>Няма установено значително намаляване на кръвния поток</li> </ul> <p>Макроскопски данни за интегриране и разграждане (клас 0-4)</p> <p><u>Каротидни места</u></p> <p><u>Вътрешна страна</u></p> <p>-капсулиране</p> <p>12 седмица 1,3</p> <p>24 седмица 0,8</p> <p>36 седмица 0,7</p> <p>-разграждане на материала</p> <p>12 седмица 2,2</p> <p>24 седмица 2,3</p> <p>36 седмица 0,7</p> <p><u>Външна страна</u></p> <p>-капсулиране</p> <p>12 седмица 2,0</p> <p>24 седмица 1,0</p> <p>36 седмица 0,8</p> <p>-разграждане на материала</p> <p>12 седмица 2,0</p> <p>24 седмица 2,7</p> <p>36 седмица 3,2</p> <p><u>Феморални места</u></p> <p><u>Външна страна</u></p> <p>-капсулиране</p> <p>12 седмица 1,0</p> <p>24 седмица 2,7</p> <p>36 седмица 1,0</p> <p>-разграждане на материала</p> <p>12 седмица 2,0</p> <p>24 седмица 2,4</p> <p>36 седмица 3,0</p> |
|--|--|--|--|------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | <p><i>Вътрешна страна</i></p> <p>-капсулиране</p> <p>12 седмици 2,0</p> <p>24 седмици 1,2</p> <p>36 седмици 1,0</p> <p>-разграждане на материала</p> <p>12 седмици 1,0</p> <p>24 седмици 2,2</p> <p>36 седмици 3,0</p> <p><u>Хистологични данни за параметри на интегриране, разграждане и възпаление (средна стойност на съответните стойности, индекс 0-4) бр.=6</u></p> <p><u>Каротидни места</u></p> <p>Външна фиброза</p> <p>12 седмици – 2,3</p> <p>24 седмици – 2,3</p> <p>36 седмици – 1,8</p> <p>Вътрешна неоинтима</p> <p>12 седмици – 3,0</p> <p>24 седмици – 2,7</p> <p>36 седмици – 3,3</p> <p>Разграждане на материала</p> <p>12 седмици – 1,7</p> <p>24 седмици – 3,0</p> <p>36 седмици – 3+</p> <p>Възпалителни параметри (макрофаги)</p> <p>12 седмици – 3,0</p> <p>24 седмици – 1,7</p> <p>36 седмици – 1,7</p> <p><u>Феморални места</u></p> <p>Външна фиброза</p> <p>12 седмици – 1,3</p> <p>24 седмици – 1,5</p> <p>36 седмици – 1,7</p> <p>Вътрешна неоинтима</p> <p>12 седмици – 3,7</p> <p>24 седмици – 3,3</p> <p>36 седмици – 3,8</p> <p>Разграждане на материала</p> <p>12 седмици – 2,0</p> <p>24 седмици – 3,0</p> <p>36 седмици – 3+</p> <p>Възпалителни параметри (макрофаги)</p> <p>12 седмици – 3,5</p> |
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|                                                                                                                                                                                       |                                                                             |                         |                                                                                                                                                                                                                    |                                                                                                                           | <p>24 седмици – 1,8<br/>36 седмици – 1,8</p> <p><u>Стойности на хистоморфологична проходимост</u></p> <p>Каротидни места<br/>12 седмица 74,0%<br/>24 седмица 81,9%<br/>36 седмици -89,43%</p> <p>Феморални места<br/>12 седмица – 42,2%<br/>24 седмица – 73,21%<br/>36 седмици – 78,71%</p> <p><u>УЗ съдова проходимост (средно %)</u></p> <p>Каротидни места<br/>12 седмица 94,6%<br/>24 седмица – 96,7%<br/>36 седмица – 94,7%</p> <p>Феморални места<br/>12 седмица – 66,9%<br/>24 седмица – 63,6%<br/>36 седмица – 75,1%</p> <p>Заклучения</p> <ul style="list-style-type: none"> <li>• Не е открит значим признак на локална непоносимост (липса на видими възпалителни, некротични или дегенеративни лезии) към 12, 24 или 36 седмици</li> <li>• Не е регистрирана значима нежелана тъканна реакция по отношение на приемателя и изделието</li> <li>• Разграждането на импланта е почти пълно към 36-та седмица</li> </ul> |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, | 2002 г.<br><br>Radi Medical System AB<br><br>Изпълнен от Biomatech, Франция | Проучване върху животни | Целта на проучването беше да се оцени биосъвместимостта и биофункционалността на биоразградим имплант, предназначен за постигане на хемостаза в съдовата система. Тестваното изделие беше предназначено да влезе в | Периодът на имплантиране / проследяване е 5 седмици за всички животни<br><br>4 овце, 1 прасе<br><br>14 затварящи елемента | Бяха записани всички критерии за нежелани признаци (възпаление, некроза, кръвоизлив или лезия) или всяко образуване на тънък псевдо-интимален слой. Особено внимание беше отделено на първоначалната тъканна                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |

|                                                                                |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
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| <p>(R1052-01) 2002, Radi Medical System AB (performed by Biomech, France).</p> |  | <p>отвора на пункцията на артерията, за да се постигне хемостаза. Единият диск влиза в отвора на пункцията на артерията, а другият затяга вътрешния диск от външната страна на артерията. И двата диска се поставят през въвеждащ катетър. Дисковете са предназначени да предотвратят кръвоизлив, да зараснат към съдовата стена и накрая да се разградят и да се абсорбират. Проучването беше предназначено да събере и анализира данни след функционална имплантация при овце и прасета, за да оцени способността на импланта да поддържа физиологична функция, когато се използва в кръвоносната система, да се определи реакцията на приемателя и реакцията на изделието (физическа цялост, тъканно капсулиране при умъртвяването) и да се оцени разграждането на импланта</p> | <p>8 затварящи елемента, имплантирани на 2 овце, 2 затварящи елемента, имплантирани на 1 прасе</p> <p>Когато два затварящи елемента се имплантират в една и съща феморална артерия, те се имплантират на разстояние &gt; 30 mm</p> | <p>интеграция на изделието, със специален акцент върху вътрешното капсулиране на диска.</p> <p>Макроскопски не се наблюдават значими признаци на локална непоносимост или образуване на тромби. Макроскопското наблюдение не разкри никаква разлика между овцете и прасето след имплантиране на затварящите елементи във феморалните артерии. Макроскопски не се наблюдават значими признаци на локална непоносимост или образуване на тромби. Макроскопското наблюдение не разкри никаква разлика между овцете и прасето след имплантиране на затварящите елементи във феморалните артерии.</p> <p>При хистопатологичния анализ на мястото на имплантиране при овцете не бяха установени локални нежелани реакции. Вътрешните и външните дискове показваха признаци на разграждане и в някои случаи бяха счупени на по-малки части. Вътрешните дискове бяха напълно интегрирани в неоинтималната тъкан. При прасето хистопатологичният анализ показва малко повече възпалителни признаци около вътрешните и външните</p> |
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|                                                                                                                                                                                                              |                              |                                                |                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                              | <p>дискоте. И при двата вида животни в мултифиламентите се установиха малко повече възпалителни признаци отколкото в материала на диска, което е нормално за плетени шевове поради по-голямата повърхност.</p> <p>Проходимостта на съда се измери след 5 седмици, като се използваха три различни метода: хистоморфометричен, хистоморфометричен в комбинация с измерване на диаметъра на съда с помощта на дебеломер и с помощта на цветна доплерова ехография. Средната проходимост на съдовете при овцете беше между 60 и 80 % в зависимост от метода (12 наблюдения). При прасето средната проходимост на съдовете беше между 40 и 80 % (2 наблюдения).</p> |
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| <b>Първо клинично проучване при хора</b>                                                                                                                                                                     |                              |                                                |                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Име на проучването                                                                                                                                                                                           | Година/CI                    | Тип на проучването                             | Цели                                                                                                                                                                                                                                                                                                | Основни етапи                                                                                                                                                                                                                                                                                                                | Потенциални критерии за приемане                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Отворено, многоцентрово изпитване с една група | Целите на проучването бяха да се определи безопасността, действието и ефективността на FemoSeal Vascular Closure System (FemoSeal System) като цяло и по-специално на затварящите елементи при пациенти, подложени на сърдечна диагностика или интервенционални кардиологични процедури, използващи | <p>Проучване в 2 части</p> <p>Общ бр.= 80</p> <p>Част 1 бр.=20</p> <p>Част 2 бр.=60</p> <p>Показания:</p> <p>Част 1 – диагностична сърдечна катетеризация с използване на феморалната артерия като място за достъп</p> <p>Част 2 – пациенти, подложени на диагностични и интервенционални сърдечни процедури, използващи</p> | <p>Резултати</p> <p><u>Хемостаза постигната с FS без компресия</u></p> <p>- Част 1 20/20 (100%)</p> <p>- Част 2 58/60 (97%)</p> <p>Средно време до хемостаза по време на процедурата (част 2) – 1,0 минути (непосредствен диапазон – 8 минути)</p> <p><u>Време до раздвижване (минути)</u></p> <p>Част 1 -</p> <p>Медиана: 33,0</p>                                                                                                                                                                                                                                                                                                                             |

|  |  |  |                                |                                        |                                                                                                                                                                             |
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|  |  |  | достъп до феморалната артерия. | феморална артерия като място за достъп | средно: 67,8                                                                                                                                                                |
|  |  |  |                                | 30-дневно проследяване                 | Част 2 -<br>медиана: 45<br>средно: 87,5                                                                                                                                     |
|  |  |  |                                |                                        | <u>Честота на големи съдови усложнения – 30-дневно проследяване</u>                                                                                                         |
|  |  |  |                                |                                        | Част 1                                                                                                                                                                      |
|  |  |  |                                |                                        | -Без съдови усложнения<br>20/20 (100%)                                                                                                                                      |
|  |  |  |                                |                                        | Част 2                                                                                                                                                                      |
|  |  |  |                                |                                        | Псевдоаневризма - 1/59<br>(1,69%)                                                                                                                                           |
|  |  |  |                                |                                        | <u>Неуспешно лечение</u>                                                                                                                                                    |
|  |  |  |                                |                                        | Част 1 – 0/20 (0%)                                                                                                                                                          |
|  |  |  |                                |                                        | Част 2 – 3/60 (5%)                                                                                                                                                          |
|  |  |  |                                |                                        | <ul style="list-style-type: none"> <li>2 поради непостигане на хемостаза без използване на компресия</li> <li>1 поради голямо съдово усложнение, псевдоаневризма</li> </ul> |
|  |  |  |                                |                                        | <u>Персистиращо изтичане</u>                                                                                                                                                |
|  |  |  |                                |                                        | Част 1 – 0/20 (0%)                                                                                                                                                          |
|  |  |  |                                |                                        | Част 2- 8/60 (13%)                                                                                                                                                          |
|  |  |  |                                |                                        | <u>Хематом</u>                                                                                                                                                              |
|  |  |  |                                |                                        | Част 1 – 0/20 (0%)                                                                                                                                                          |
|  |  |  |                                |                                        | Част 2 – 6/60 (10%)                                                                                                                                                         |

Като част от предпазарния план за разработване на FemoSeal VCS бяха завършени 3 функционални теста върху животни. През 2000 г., преди започването на клиничните проучвания, беше проведено изследване върху животни за оценка на биофункционалността на FemoSeal™ VCS. Това проучване оцени способността на затварящите елементи да поддържат физиологичната функция и тяхното разграждане. Към 18-я месец материалът на вътрешния и външния диск вече не се виждаше, като беше заменен с ендолуминална фиброзна тъкан. В заключение, беше потвърдена способността

на затварящия елемент FemoSeal™VCS да поддържа физиологичната функция, когато се използва в кръвоносната система.

През 2002 г. беше проведено проучване върху животни за оценка на биосъвместимостта и биофункционалността на биоразградим имплант, FemoSeal™VCS, предназначен за постигане на хемостаза в съдовата система. В резюме, разграждането на импланта беше почти пълно към 36-та седмица и нямаше значима нежелана тъканна реакция.

Друго проучване върху животни през 2002 г. оцени биосъвместимостта и биофункционалността на биоразградим имплант, FemoSea™ VCS, предназначен за постигане на хемостаза в съдовата система. След 5 седмици капсулирането на диска беше завършено и бяха наблюдавани признаци на разграждане за вътрешните и външните дискове. В заключение, беше потвърдена способността на импланта да поддържа физиологичната функция, когато се използва в кръвоносната система.

Като част от плана за клинично разработване на FemoSeal™ VCS, Radi Medical System AB проведе клинично проучване преди пускане на пазара. Това клинично изследване не е публикувано, нито е достъпно онлайн. Изследването с модел на устройството № 11200 беше проведено през 2002-2004 г. съгласно европейски стандарт EN 540 (Клинично изследване на медицински изделия за хора) и в съответствие с общите съображения на ICH за клинични изпитвания и насоките за добра клинична практика. Подробностите за това проучване са документирани в доклад EU-SE-001. Клиничното изпитване е документирано в окончателния доклад на Radi Medical Systems AB, „Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures“. Клиничното проучване е проведено с първия модел № 11200 на FemoSeal™ и е фокусирано върху безопасността и ефективността на имплантируемите компоненти за затваряне. Единствената разлика между първия модел № 11200 и настоящия модел, C11202, е френският размер, съответно 6F и 7F, и подобрената система за доставка. Клиничните ползи, предназначението, принципите на работа и суровините на имплантируемите затварящи елементи, вътрешното уплътнение и външния заключващ диск остават непроменени.

Предназначението на изделието е за пациенти, подложени на сърдечни диагностични или интервенционални процедури, използващи феморалната артерия като точка за достъп. Целта на това проучване беше да се определи безопасността, действието и ефективността на FemoSeal™ VCS. Това беше проспективно, многоцентрово, отворено проучване с една група с 30-дневно проследяване.

Първичният очакван резултат за клиничното действие беше времето до хемостаза, определено като липса на обилно кървене. Първичният очакван резултат за безопасността беше честотата на сериозни съдови усложнения в рамките на 30 дни. Вторичните очаквани резултати включваха време до раздвижване, процент на неуспешните



процедури, честота на нежеланите събития и характеристики на работата на изделието по време на доставка и поставяне.

Пациентите, включени в това проучване, бяха възрастни, способни да дадат информирано съгласие и с поне един незасегнат пулс на стъпало. Пациенти с някои от следните състояния бяха изключени от проучването:

- Анамнеза за периферно съдово заболяване
- Автоимунно заболяване
- Известно нарушение на кръвосъсирването или тежка анемия
- INR >1,5
- Инфаркт на миокарда през последните 72 часа
- Неконтролирана хипертония въпреки лечението
- Затлъстяване, което изключва достъп с техниката на Seldinger
- Пациенти със съдов графт или стент на мястото на артериотомия
- Предишна ипсилатерална пункция през последните 3 месеца
- Очаквана продължителност на живота < 6 месеца

Освен това пациентите бяха прегледани интраоперативно и бяха изключени от проучването при установяване на някои от следните:

- Диаметър на лумена на общата феморална артерия < 5 mm
- Артериални разклонения в рамките на 2 cm проксимално от мястото на пункцията
- Значителна стеноза в рамките на 3 cm от мястото на пункцията
- Използване на първичен въвеждащ катетър > 6Fr
- Пункция върху или дистално от бифуркацията на феморалната артерия
- Множество пункции във феморалната артерия
- Известна или подозирана пункция на задната стена на феморалната артерия
- Голям хематом (2:6 cm) при завършване на процедурата
- Трудно поставяне на първичния процедурен катетър поради изкривена тъкан или съд

Това проучване с един протокол се проведе в две части: 20 пациенти бяха включени в част 1, след което беше извършен анализ на безопасността и след това бяха включени допълнителни 60 пациенти по време на част 2.

В част 1 средната възраст на включените пациенти беше 65,9 години, 70,0% от пациентите бяха мъже и 95% от пациентите бяха на съпътстващи лекарства. В част 2 на проучването средната възраст беше 63,8 години, 78% бяха мъже и 100% бяха на съпътстващи лекарства.

Пациенти, подложени на диагностични (част 1 и част 2) или интервенционални (част 2) процедури за сърдечна катетеризация, отговаряха на условията за включване в проучването. Процедурите бяха в съответствие със стандарта за грижи във всяка от участващите болници, последвани от използване на FemoSeal™ VCS. Данните за пациентите бяха събрани на изходно ниво, по време на процедурата и на 1-я и 30-я ден след процедурата. Резултатите са обобщени в **Таблица 1.5** и показват, че FemoSeal™ VCS е безопасна и ефективна за употреба при тази група пациенти.

**Таблица 1.5 Клинични резултати, съобщени в проучването преди пускане на пазара**

|                                                                                                               | Част 1      | Част 2                   |
|---------------------------------------------------------------------------------------------------------------|-------------|--------------------------|
| Брой пациенти                                                                                                 | 20          | 60                       |
| Средно време до хемостаза                                                                                     | 1,2 минути  | 1,6 минути <sup>a</sup>  |
| Средно време до раздвижване                                                                                   | 72,2 минути | 87,5 минути <sup>b</sup> |
| Честота на сериозни съдови усложнения <sup>c</sup>                                                            | 0 (0%)      | 1 (2%)                   |
| Брой пациенти с нежелани събития                                                                              | 5 (25%)     | 19 (32%)                 |
| Неуспешно лечението (дефинирано като сериозни съдови усложнения, необходимост от ръчна компресия или и двете) | 0 (0%)      | 3 (5%)                   |
| Неизправности на изделието                                                                                    | 0 (0%)      | 6 (10%)                  |

<sup>a</sup>На база на общия размер на извадката от 58 пациенти, тъй като 2 пациенти не са достигнали хемостаза по време на процедурата поради предишни ипсилатерални пункции. Хемостазата е постигната на 7-та минута и 37-та минута при тези пациенти.

<sup>b</sup>На база на общия размер на извадката от 59: 1 пациент не беше включен, тъй като беше поставен на изкуствено дишане поради белодробен оток и не можеше да се движи повече от седмица.

<sup>c</sup>Определя се като съдово усложнение, изискващо кръвопреливане или хирургично възстановяване, или локална инфекция, изискваща приложение на антибиотик, хоспитализация или удължаване на хоспитализацията, или дебридман на мястото

Не са наблюдавани сериозни съдови усложнения в част 1 на проучването. Имаше 1 сериозно съдово усложнение, съобщено в част 2 на проучването: псевдоаневризма, която беше съобщена в рамките на 1 ден след процедурата. Събитието наложи ултразвуково контролирана компресия и инжектиране на тромбин в псевдоаневризмата, както и удължаване на хоспитализацията на пациента.

От 5 нежелани събития, докладвани в част 1 на проучването, имаше 1 вероятно свързано с изделието нежелано събитие: несериозно събитие на обилно кървене на 1-ия ден след процедурата. От съобщените 19 нежелани събития в част 2 на проучването са наблюдавани 3 несериозни нежелани събития на хематом и 6 вероятно свързани с изделието несериозни събития, включително 3 съобщения за упорито леко кървене, 2 хематома и 1 болка в единия крак след тренировка.

В част 2 имаше 3 пациенти, които бяха определени като случаи на неуспешно лечение: 2 поради невъзможност за постигане на хемостаза без използване на компресия и 1 поради голямо съдово усложнение (псевдоаневризма). Няма установено неуспешно лечение в част 1 на проучването.

От шестте неизправности на изделието в част 2 на проучването три не попречиха на процедурата, една беше приписана на грешка на потребителя, една беше теч в катетъра и една беше скъсан филament. Последните два проблема бяха решени с актуализации на модела, внедрени в C11202.

Част 2 на клиничното проучване преди пускането на пазара не отчита резултатите от 6-месечното проследяване поради изпълнение на изискванията от страна на пациента. Резултатите от 30-дневното проследяване в клиничното проучване преди пускане на пазара (EU-SE-001), които са в съответствие с периода на проследяване в клиничната литература, показват, че FemoSeal™ VCS е безопасна и ефективна.

#### 1.4.2 Резюме на данните от клинични проучвания след пускане на пазара

В Таблица 1.6 по-долу са описани 4 завършени постмаркетингови клинични проучвания. Тези клинични изследвания не са публикувани, нито са достъпни онлайн.

**Таблица 1.6 Завършени клинични проучвания след пускане на пазара**

| Завършени клинични проучвания след пускане на пазара             |              |                                                                                     |                                                                                                                                 |                                                                                                                                                   |                                                                                           |
|------------------------------------------------------------------|--------------|-------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| Име на проучването                                               | Година/CI    | Тип на проучването                                                                  | Цели                                                                                                                            | Основни етапи                                                                                                                                     | Потенциални критерии за приемане                                                          |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of | 2006<br>RADI | Постмаркетингово проучване, приемливост на новата опаковка от страна на потребителя | Постмаркетингово проучване, извършено за актуализирания модел FemoSeal Vascular® Closure System № 11202, който има модифицирана | 100 пациенти <ul style="list-style-type: none"> <li>63 мъже / 37 жени</li> <li>Средна възраст 68 години за жените, 65 години за мъжете</li> </ul> | Резултати <p>1. Илюстрациите/ инструкциите в ИУ се считат за информативни и подходящи</p> |

|                                                                                   |                                                           |                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|-----------------------------------------------------------------------------------|-----------------------------------------------------------|---------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------|----|-----|----------|-------|----------|-----------|----|-----------|-----------|-------------------------|----------|--------------------|------------|---------------------|-----------|-------------------|---------|-----------------------|----------|--------------------------------|----------|----------------------|-----------|--------------------------|-----------|-----------------------------------|----------|----------------------|--------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| New Packaging (SIS) (2006)                                                        |                                                           |                                       | система за доставяне в сравнение с първия модел, № 11200, с цел документиране на функционалността.<br><br>Целта на проучването беше да се получи обратна връзка относно ревизираните инструкции за употреба (ИУ) и проекта за обучение на лекари и медицински сестри, да се потвърдят оценките, направени в анализа на риска, и да се набавят идеи за евентуални подобрения в качеството на продукта. | 2 болници в Швеция, 6 лекари<br><br>112 изделия<br><br>Данни, записани в клиничните карти на пациента (ККП)<br><br>Планирано време за наблюдение – 30 минути от момента на приложение                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 2. Незабавна хемостазата (91/100) |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008) | Dr. Nicolas Moes<br>Innsbruck Medical University, Австрия | Постмаркетингова потвърждаваща оценка | Целта на това проучване беше да се оцени безопасността и действието на FemoSeal®, използвана по време на нормалната клинична практика при пациенти, подложени на диагностична сърдечна катетеризация или перкутанна сърдечна интервенционална процедура, извършена с 7F-катетър.                                                                                                                      | 50 последователни пациенти<br><br>Показание – диагностична или инвазивна сърдечна катетеризация през общата феморална артерия<br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                 | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Първични крайни точки <ul style="list-style-type: none"><li>Първична крайна точка за ефикасност – ТТН (време до хемостазата) със или без леко кървене, но без допълнителна компресия, ръчна или механична.</li><li>Крайна точка за безопасност - честота на нежеланите събития - леки и сериозни съдови усложнения и всички други нежелани събития - сериозни и несериозни, за периода на проучването (т.е. до изписването на пациента).</li></ul> Резултати <ul style="list-style-type: none"><li>Средно време до хемостазата</li><li>Диагностика - 56,6 ± 29 секунди</li><li>Интервенции 59,9 ± 16,2 секунди</li><li>Всички пациенти 57,8± 26,3</li><li>Всички пациенти могат да бъдат раздвижени след 4 часа почивка на легло без никакви проблеми.</li></ul> Резултати за безопасност <ul style="list-style-type: none"><li>49/50 (98%) без съдови усложнения до изписване от болницата</li></ul> |
| n                                                                                 | 50                                                        |                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| men                                                                               | 35 (70%)                                                  |                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| women                                                                             | 15 (30%)                                                  |                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| PCI cases                                                                         | 15                                                        |                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| age (yrs)                                                                         | 62.8±11.1                                                 |                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| body mass index (kg/m²)                                                           | 25.4±6.7                                                  |                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| systolic BP (mmHg)                                                                | 131.2±20.9                                                |                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| diastolic BP (mmHg)                                                               | 77.9±10.6                                                 |                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| diabetes mellitus                                                                 | 9 (18%)                                                   |                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| arterial hypertension                                                             | 34 (68%)                                                  |                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| previous coronary intervention                                                    | 13 (26%)                                                  |                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| preprocedure aspirin                                                              | 50 (100%)                                                 |                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| preprocedure clopidogrel                                                          | 50 (100%)                                                 |                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Procedural unfractionated heparin                                                 | 15 (30%)                                                  |                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Procedural abciximab                                                              | 2 (4%)                                                    |                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |

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|                                                                                                                                 |                                 |                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                               | <ul style="list-style-type: none"> <li>Средно време до изписване 2,6 дни</li> <li>1/50 (2%) с леко кървене на следващия ден след безпроблемно раздвижване в деня на ангиографията</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | 2009 RADI                       | Постмаркетингово проучване                                  | <p>Проучването трябва да даде информация дали клиентите/потребителите са забелязали някакви проблеми с новата опаковка, особено с нестерилната външна страна на торбичката Tuvek/PET-PE.</p> <p>Проучването трябва също така да предостави информация за това дали лекуващият лекар е забелязал някакви разлики в стъпките за прилагане/поставяне на изделието в сравнение с използваните преди това изделия.</p> <p>Проучването трябва също да даде информация за необходимостта от допълнително подобряване на качеството на продукта.</p> | <p>25 изделия</p> <p>4 болници в Швеция</p> <p>16/25 (64%) от пациентите са пациенти с PCI на силни антикоагулационни лекарства</p>                                                                                                                                                                                                           | <p>Резултати</p> <ol style="list-style-type: none"> <li>Проблеми, свързани с опаковката – 21/25 (84%) приложения са били успешни; 4/25 (16%) са били неуспешни (1 - тестване на нов водещ катетър, 1 вътрешен диск преминава през хода на артериотомия, при изтеглянето бутонът се връща обратно и външният диск се поставя в тъканния канал на разреза, 2 не беше постигната незабавна хемостаза въпреки липсата на проблеми с поставянето.)</li> <li>Незабавна хемостаза 19/25 (76%) пациенти</li> <li>Кървене 11/25 (44%) – 9/25 (36%) леко изтичане/кървене, 2/25 (8%) хематоми</li> </ol> <p>Общ процент на събития 19%</p> |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022) | 2022/Terumo Medical Corporation | Проспективно, многоцентрово, наблюдателно, постмаркетингово | Допълнително да демонстрира безопасността и ефективността на FemoSeal™ VCS при постигане на хемостаза на местото за достъп през общата феморална артерия (CFA) при пациенти в реална среда, подложени на перкутани ендоваскуларни процедури                                                                                                                                                                                                                                                                                                  | <ul style="list-style-type: none"> <li>Проследяване на пациента след 30 дни (<math>\pm</math> 7 дни) чрез посещение в болницата или телефонно обаждане.</li> <li>Включване: от декември 2021 г. до юли 2022 г.</li> <li>230 включени участници, подложени на диагностични или интервенционални ендоваскуларни процедури, при които</li> </ul> | <ul style="list-style-type: none"> <li><b>Демографски данни/съпътстващи заболявания:</b> <ul style="list-style-type: none"> <li>- Пол: 161 мъже (70%)/69 жени 69 (30%).</li> <li>- Средна възраст: 70 <math>\pm</math> 12.</li> <li>- BMI (индекс на телесната маса): 26,1 <math>\pm</math> 4,95 kg/m<sup>2</sup>.</li> <li>- Хипертония: 160 пациенти (69,6%).</li> <li>- Дислипидемия: 128 (55,7 %).</li> <li>- Коронарна артериална болест: 42 (18,3%).</li> </ul> </li> </ul>                                                                                                                                                |

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|  |  |  |  | <p>се използва AFemoSeal™.</p> <p>3 европейски центъра: Франция (92 пациента), Германия (38 пациента), Белгия (100 пациента).</p> | <ul style="list-style-type: none"> <li>- Настоящи пушачи: 86 (37,6%).</li> <li>- Пушачи в миналото: 66 (28,8%).</li> <li>- Коронарна болест на сърцето: 34 (14%).</li> <li>- Предишен инфаркт на миокарда: 18 (7,8%).</li> <li>- Реваскуларизация на периферна артерия: 12 (5,2%) каротидна артерия и 83 (37,5%) и артерия на долния крайник.</li> <li>- Антитромбоцитна терапия (при изходно ниво): 211 (91,7%), включително 21 (9,1%) двойна антитромбоцитна терапия (DAPT).</li> <li>- Перорална антикоагулация: 40 (17,4%) пациенти.</li> <li>• <b>Характеристики на интервенцията:</b> <ul style="list-style-type: none"> <li>- Условия: болнична клиника 162 случая (70,4%), амбулаторна клиника 68 случая (29,6%).</li> <li>- Преобладаващо показание: клаудикация 147 случая (63,9%).</li> <li>- Подход: 35 антероградни (15,3%), 194 ретроградни (84,7%).</li> </ul> </li> <li>• <b>Първични крайни точки:</b> <ul style="list-style-type: none"> <li>- Комбинираната крайна точка за безопасност (липса на сериозни усложнения на крайника на мястото на достъп в рамките на 6 часа след процедурата) и ефективност (успешна хемостаза на мястото на пункцията) е постигната при 215/226 (95,1%) [95% ДИ: 91,46;</li> </ul> </li> </ul> |
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|  |  |  |  |  | <p>97,55] пациенти в групата за пълен анализ и 215/230 (93,5%) [95% ДИ 89,47, 96,30] в групата с лечение с FemoSeal™.</p> <p>- Крайната точка за ефективност беше постигната при 219/226 (96,9%) ДИ [93,7, 98,7] пациенти.</p> <p>- Крайната точка за безопасност беше постигната при 220/230 (95,2%) [95% ДИ: 92,15, 97,90] пациенти.</p> <p>• <b>Вторични крайни точки:</b></p> <p>- Липса на незначителни усложнения на мястото на достъп за шест часа след процедурата, постигната при 225/230 (97,8%) [95% ДИ: 95,00; 99,29].</p> <p>- Липса на големи и малки усложнения на мястото на достъп от шест часа до 30 дни след процедурата, постигната при 219/230 (95,2%) [95% ДИ:91,60; 97,59] пациенти.</p> <p>- Средно време до хемостаза с FemoSeal™ VCD: 0,42 (0,25; 0,50) минути.</p> <p>- Средно време до амбулация: 5,00 (4,54; 5,50) минути.</p> <p>- Медиана на престоя в болницата: 23,98 (22,72, 25,00) часа.</p> <p>- Използваемост на FemoSeal™ VCS: „лесно“ или „много лесно“ за поставяне в 98,7% от случаите ("лесно" за поставяне в 21 (9,2%), „много лесно“ за поставяне в 205 (89,5%)) с никакво</p> |
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|  |  |  |  |  | или слабо съпротивление при поставяне в 226 (98,3%) от случаите.<br>152/230 (66,1%) от пациентите, лекувани с водача, включен в комплекта FemoSeal™ (GW 0,038") и препоръчан в FemoSeal™, без докладвани недостатъци на изделието или нежелани събития. |
|--|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Проучването през 2006 г. беше проведено, за да се потвърди безопасността и ефективността на настоящото изделие с подобрена система за доставяне и да се получи обратна връзка относно ИУ и програмата за обучение на FemoSeal™ VCS. Проучването включваше 100 пациенти и първичната крайна точка беше дали е постигната хемостаза или са необходими допълнителни ръчни или механични компресии. Това проучване заключава, че приложението на FemoSeal™ VCS е било успешно в повечето случаи (при 91% е постигната незабавна хемостаза).

Проучването през 2008 г. включваше 50 пациенти за оценка на безопасността и ефективността на FemoSeal™ VCS, когато се използва по време на нормална клинична практика при пациенти, подложени на сърдечна катетеризация с катетър 7 Fr. Първичната крайна точка на проучването беше да се съберат данни за времето до хемостаза и времето до раздвижване без допълнителна компресия, ръчна или механична. Резултатите от проучването показаха, че средното време за хемостаза е 57,8 секунди и всички пациенти са се раздвижили след 4 часа почивка на легло.

Проучването през 2009 г. беше за оценка на новата опаковка на FemoSeal™ VCS. В проучването бяха включени 25 пациенти. Първичната крайна точка беше дали потребителят е имал проблеми с опаковката. Потребителите не отбелязаха проблеми по отношение на новата опаковка на FemoSeal™ VCS. Това проучване също събираще данни за времето до хемостаза.

Целта на проучването от 2022 г. беше да събере проактивно данни за безопасността и ефективността на FemoSeal VCS при постигане на хемостаза на мястото за достъп през общата феморална артерия (CFA) при пациенти в реална среда, подложени на перкутанни ендоваскуларни процедури. В проучването бяха включени 230 пациенти. Първичните крайни точки за регистъра са успех на процедурата (т.е. успешна хемостаза на мястото на пункцията) и намаляване на сериозните усложнения (напр. съдово увреждане, кървене, свързано с мястото на достъп, инфекция на мястото на достъп, повторна ръчна компресия и нова остра ипсилатерална исхемия на крака, свързана с мястото на достъп). Проучването



заклучи, че FemoSeal VCS функционира добре в реални условия и осигурява ефективна хемостаза и ниски нива на усложнения на мястото на достъп за пациенти, подложени на периферни ендоваскуларни интервенции. Беше демонстрирана добра ефективност с кратко време до хемостаза и добра обратна връзка за удобството на оператора, което прави FemoSeal VCS ценно изделие за затваряне на феморален достъп.

### 1.4.3 Резюме на данните от клинични проучвания след пускане на пазара

#### 1.4.3.1 Завършени постмаркетингови клинични проследявания

Обобщение на завършените дейности за клинично проследяване след пускане на пазара е описано в Таблица 1,7 по-долу.

**Таблица 1.7. Постмаркетингови дейности за клинично проследяване**

| Завършени постмаркетингови клинични проследяващи дейности                 |             |                                                                         |                                                                                                                                                                                                       |                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|---------------------------------------------------------------------------|-------------|-------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Име на дейността                                                          | Година / CI | Тип на проучването                                                      | Цели                                                                                                                                                                                                  | Основни етапи                                                                                                                                                                                         | Потенциални критерии за приемане                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021 TMC    | Клинично проучване след пускане на пазара - висококачествен о проучване | Проучване след пускане на пазара за събиране на проспективна обратна връзка, свързана с използването на изделието за затваряне на съдове FemoSeal™, разпространявано на пазарите на Европейския съюз. | <ul style="list-style-type: none"> <li>120 случая</li> <li>8 уникални лекари с &gt; 5 години опит</li> <li>Няколко държави в Европа</li> </ul>                                                        | <p><b>Оценки на устройството по скала 1-5 – Изявления от анкетата</b></p> <ul style="list-style-type: none"> <li>Критерии за приемане <ul style="list-style-type: none"> <li>Оценките 3-5 се считат за благоприятни</li> <li>Всички изявления трябва да имат <math>\geq 80\%</math> положителна обратна връзка</li> </ul> </li> <li>Резултати <ul style="list-style-type: none"> <li>Не е получено изявление в анкетата с &gt; 20% неблагоприятна обратна връзка</li> <li>Няма подадени оплаквания за продукта</li> </ul> </li> </ul> |
| 20210298 – 0.035” and 0038” Guidewire Clinical Survey Report (2021)       | 2021 TMC    | Клинично проучване след пускане на пазара - висококачествен о проучване | Проучване след пускане на пазара за събиране на проспективна обратна връзка, свързана с използването на жичния водач 0,035”, включен в                                                                | <ul style="list-style-type: none"> <li>Проучвания за 0,035” кабел <ul style="list-style-type: none"> <li>106 проучвания</li> <li>64 лекари</li> </ul> </li> <li>Проучвания за 0,038” кабел</li> </ul> | <p><b>Оценки на устройството по скала 1-5 – Изявления от анкетата</b></p> <ul style="list-style-type: none"> <li>Критерии за приемане <ul style="list-style-type: none"> <li>Оценките 3-5 се считат за благоприятни</li> <li>Всички изявления трябва да имат <math>\geq</math></li> </ul> </li> </ul>                                                                                                                                                                                                                                 |

| Завършени постмаркетингови клинични проследяващи дейности                                                                       |                         |                                                                         |                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
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|                                                                                                                                 |                         |                                                                         | 6Fr Angio-Seal™ VIP Vascular Closure Device (VCD), и 0,038", включен в 8Fr Angio-Seal™ VIP VCD и FemoSeal Vascular Closure System, разпространявани на пазарите на Европейския съюз. | <ul style="list-style-type: none"> <li>○ 109 проучвания</li> <li>○ 55 лекари</li> <li>• 12 ретроспективни проучвания</li> </ul>                                                                                                                                                                                                                                      | <p>80% положителна обратна връзка</p> <ul style="list-style-type: none"> <li>• Резултати <ul style="list-style-type: none"> <li>○ Всички жични водачи са получили приемливи оценки</li> <li>○ Няма подадени оплаквания за продукта</li> </ul> </li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024<br><br>TMC/TE | Клинично проучване след пускане на пазара - висококачествен о проучване | Проспективно събиране на обратна връзка, свързана с използването на FemoSeal VCS с жични водачи, разпространявани на пазара на ЕС.                                                   | <ul style="list-style-type: none"> <li>• 126 проучвания <ul style="list-style-type: none"> <li>• 7 обекта</li> <li>• 5 държави</li> </ul> </li> <li>• 14 ноември 2023 г. - 11 юни 2024 г.</li> <li>• Медицински специалист: <ul style="list-style-type: none"> <li>○ Съдов хирург</li> <li>○ Интервенционен рентгенолог</li> <li>○ Ангиология</li> </ul> </li> </ul> | <p><b>Оценки на устройството по скала 5 – Изявления от анкетата</b></p> <ul style="list-style-type: none"> <li>• Критерии за приемане <ul style="list-style-type: none"> <li>○ Оценките 3-5 се считат за благоприятни</li> <li>○ Всички изявления трябва да имат ≥ 80% положителна обратна връзка</li> <li>○ Ако в това проучване възникнат нежелани събития, те трябва да бъдат тези, предвидени от управлението на риска.</li> </ul> </li> <li>• Демографски характеристики на пациентите: <ul style="list-style-type: none"> <li>○ Жени 29,4% (37/126)</li> <li>○ Мъже 69,8% (88/126)</li> <li>○ Полът не е посочен: 0,8 (1/126)</li> <li>○ Възраст &gt;75 години: 31,7%</li> </ul> </li> <li>• Резултати <ul style="list-style-type: none"> <li>○ Жичен водач, доставен с</li> </ul> </li> </ul> |

| Завършени постмаркетингови клинични проследяващи дейности |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|-----------------------------------------------------------|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                           |  |  |  |  | <p>FemoSeal™ VCS: 101/126 (80,2%).</p> <ul style="list-style-type: none"> <li>○ Продължителност на процедурата (минути): 63,4 (36,6) (средно (SD)); 57,0 (36,0-81,0) (медиана (IQR))</li> <li>○ Всички оценки на ефективността на FemoSeal™ VCS бяха благоприятни.</li> <li>○ Всички оценки на водача, доставян с FemoSeal™ VCS, бяха благоприятни.</li> <li>○ Едно нежелано събитие (0,8%): дисковете на FemoSeal™ VCS не бяха правилно подравнени вероятно поради използването на твърд жичен водач (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 inch), изискващ ръчна компресия за постигане на хемостаза.</li> </ul> |

Terumo Medical Corporation попълни три висококачествени проучвания на потребителите-лекари през текущия отчетен период (01 септември 2019 г. - 31 август 2024 г.).

Клиничните анкети за FemoSeal™ събраха проактивни клинични данни във връзка с безопасността и действието на FemoSeal™ VCS по време на клинична употреба.

Анкетата включваше въпроси, насочени към цялостното изделие и свързаните аксесоари, включително 0,038-инчовия водач, както и техните преки взаимодействия. Клиничните

анкети за водача събраха проактивни клинични данни по отношение на безопасността и действието по време на клинична употреба на 0,038-инчовия водач, доставен с FemoSeal™ VCS. Въпросите в анкетата бяха насочени конкретно към общата употреба на водача, от поставянето през процедурния катетър в съда до отстраняване на водача.

FemoSeal™ VCS и 0,038-инчовия водач, включен към изделието, получиха приемливи оценки, като бяха подадени шест (6) оплаквания за изделието и девет (9) несъответствия, свързани с водача, въз основа на оценка на коментарите, получени от висококачествените клинични анкети. Беше направена оценка на оплакванията както за FemoSeal, така и за водача, и те бяха анализирани като част от процеса на постмаркетингово наблюдение на Terumo. Няма установени нови рискове и/или нива на риск.

През 2024 г. беше завършено проучване на потребителите на лекари като част от дейностите по PMCF. Резултатите от проучването показаха, че оценката на ефективността и безопасността на FemoSeal™ VCS като цяло са много благоприятни. Съвместимостта на жични водачи, различни от стандартния, предоставен с FemoSeal™ VCS, също е демонстрирана.

#### **1.4.3.2 Текущо/планирано клинично проследяване след пускане на пазара**

ТМС има едно текуща/планирана дейност за постмаркетингово клинично проследяване. Ще бъде проведена клинична анкета за проспективно получаване на обратна връзка по отношение на използването на водача с FemoSeal VCS, разпространяван на пазара на ЕС. Анкетата ще бъде попълнена от лекарите, за да се проучи кои водачи са използвали по време на процедурата. Целта на това проучване е да се отстрани пропуск, идентифициран като липса на литература и коментари от външни рецензенти относно съвместимостта на FemoSeal™ VCS с използването на други жични водачи от други марки, различни от Terumo. Обратната връзка включва технически резултати, клинично представяне и безопасност, свързани с работата на изделието с различни водачи.

#### **1.4.4 Резюме на данните от систематичния преглед на литературата**

Terumo Medical Corporation провежда системни прегледи на литературата, за да събере и оцени клиничните данни за безопасност и ефективност от публикувани проучвания на FemoSeal™ VCS и/или подобни устройства. Целта на ежегодния преглед на публикуваната литература е да се идентифицират неизвестни досега странични ефекти, да се наблюдават известните странични ефекти, да се идентифицират възникващи рискове и да се идентифицира евентуална системна злоупотреба или употреба не по предназначение на AFemoSeal™ VCS.

Най-скорошният системен преглед на литературата, който обхваща периода от 1 септември 2019 г. до 31 август 2024 г., идентифицира 29 публикувани проучвания, които предоставят данни за клинична безопасност и ефективност на устройството FemoSeal™ VCS. В девет проучвания са докладвани двадесет и три референции за употреба на FemoSeal™ VCS върху етикета и употреба извън етикета. Като цяло прегледът на литературата от проучвания, специфични за употребата на FemoSeal™ VCS, показва изследвана популация, която е представителна за пациентите в ЕС, подложени на процедури за перкутанна съдова катетеризация. Вижте **Раздел 3** за списък на тези 23 рецензирани публикации.

Клиничното представяне беше оценено чрез следните мерки:

- Времето до хемостаза е по-добро или сравнимо с най-съвременните технологии за перкутанно затваряне на феморална артерия.
- Времето до раздвижване е по-добро или сравнимо с най-съвременните технологии за перкутанно затваряне на феморална артерия.
- Процентът на следоперативните усложнения е сравним или по-нисък от настоящите стандарти за грижа.

Въз основа на тези мерки за клинично действие данните в този преглед на литературата показват, че FemoSeal™ VCS може да се използва успешно при затваряне на пункция на феморалната артерия (артериотомия) при пациенти, които са претърпели перкутанна катетеризация с използване на 7 Fr или по-малък процедурен катетър. Пълна хемостаза беше постигната при мнозинството пациенти (79,65-100%) от случаите и беше свързана със средно време до хемостаза от 0,5 минути, средно време до изписване от 3 дни. Между 69,2 и 86,7% от пациентите бяха в състояние да се движат 5 часа след затварянето, със средна постоперативна почивка в леглото от 349 минути. Неизправност на FemoSeal™ VCS е наблюдавана в 3,68 - 4% от случаите, а допълнителна ръчна компресия е била необходима в 0,9 - 4,4% от процедурите.

Клиничната безопасност беше оценена чрез нежеланите събития, включително, но не само:

- Кървене
- Хематом
- Псевдоаневризма
- Синина
- Артериовенозна фистула
- Инфекция
- Смърт

За всяко от тези нежелани събития честотата на възникване, докладвана за FemoSeal™ VCS във включените проучвания, е по-ниска или сравнима с исторически докладваните честоти при ръчна компресия и други устройства за затваряне на съдове.

Не бяха идентифицирани нежелани събития при прегледа на 10 съобщения за случаи, тъй като не бяха идентифицирани нови, неочаквани, възникващи или неприемливи рискове.

Общата ефективност на използването на FemoSeal™ VCS по време на диагностична ангиография или интервенционални операции зависи от множество фактори, като пол, възраст, анатомия на пациента, съпътстващи заболявания, анатомично разположение на мястото на пункцията, опит на хирурга, метод на поставяне на VCD, следоперативни грижи, и др. В допълнение към техническия успех, включително постигане на хемостаза, FemoSeal™ VCS предлага КЛИНИЧНА полза по отношение на затварянето на съдовете след пункция на феморалната артерия, като например намаляване на времето до хемостаза, намаляване на времето до възстановяване. Резултатите от представянето на изследваните изделия съответстват на тези, очаквани за този тип изделие, когато се използват по предназначение. Някои от референциите, извлечени по време на текущия период на търсене, показват употребата на въпросното изделие на анатомично място, различно от общата феморална артерия, и за затваряне на артериотомии > 7 Fr, което се счита за извън етикета.

По време на прегледа не са идентифицирани неизвестни странични ефекти, възникващи рискове или възможна систематична злоупотреба с изделието. Въпреки това, ако FemoSeal™ VCS се използва внимателно от обучени лекари, медицинското изделие функционира като полезно и необходимо клинично изделие. Като цяло целевата терапия и следователно FemoSeal™ VCS отговарят на клиничната нужда, която съществува понастоящем при лечението на усложнения, свързани със съдовия достъп.

Като цяло, данните в този преглед на литературата не идентифицират никакви проблеми с ефективността или безопасността в клинична среда, които преди това са били неизвестни, нито нежелани ефекти, които са настъпили при по-високи от очакваните/приемливи проценти. Следователно от този преглед на литературата може да се заключи, че FemoSeal™ VCS, когато се използва за осигуряване на компресия за хемостаза при артериотомия след перкутанна катетеризация, продължава да работи според очакванията и не е свързана със сериозни събития по отношение на безопасността.

#### **1.4.5 Резюме на данните от клинични проучвания след пускане на пазара**

Въведена е проактивна система за постмаркетингово наблюдение (PMS) и прегледът на всички оплаквания се извършва ежемесечно и в съответствие с вътрешните производствени процедури. Данните за оплакванията бяха анализирани през периода от 1 септември 2019 г. до 31 август 2024 г. Като цяло има 28 доклада от наблюдение на медицинските изделия (MDV) и 476 доклада за оплаквания от клиенти, подадени до производителя. От 28 доклада за MDV, 27 са свързани с нежелани събития и един с неизправност на изделието. Имаше два смъртни случаи през отчетния период, но нито

един от докладваните смъртни случаи не беше определен като свързан с изследваното изделие. От 476-те оплаквания, отправени към производителя, най-честите причини за оплаквания са затруднения при разгръщането (146 случаи, 0,0142% честота на възникване). Режимът на неизправност на събитията на изтегляне е вторият най-често срещан с честота от 0,0126% (130 събития).

FemoSeal Vascular Closure System има над 1 030 136 продажби в световен мащаб и 827 843 в Европейското икономическо пространство. Изчислената честота на оплакванията въз основа на глобалните продажби е 0,046%. Общият процент на оплаквания от клиенти е много нисък. Не са установени нови рискове, които да не са включени в инструкциите за употреба и документацията за риска.

Честотата на нежеланите странични ефекти е показана в **Таблица 1.2**. Не са идентифицирани нови непредвидени, възникващи или неприемливи рискове. Не са наблюдавани значими увеличения на честотата или тежестта на известните нежелани странични ефекти.

#### **1.4.6 Общо резюме на клиничното действие и безопасността**

FemoSeal™ Vascular Closure System е предназначена за затваряне на пункция на общата феморална артерия (артериотомия) при пациенти, които са били подложени на перкутанна катетеризация с помощта на 7F (2,33 mm) или по-малък процедурен катетър. Тази клинична оценка се основава на изчерпателен анализ на наличните клинични данни и литература преди и след пускане на пазара, свързани с предназначението на FemoSeal™ VCS.

Извършен е цялостен преглед на публикуваната литература за периода от 1 септември 2019 г. до 31 август 2024 г. Доказателствата включват 29 проучвания за FemoSeal™ VCS. Доказателствата, предоставени в клиничната оценка, заключават, че когато се използва според показанията, въпросното изделие е безопасно и ефективно и всички рискове или нежелани странични ефекти, които могат да бъдат свързани с изделието при нормални условия на употреба, представляват приемливи рискове, когато се претеглят спрямо ползите за пациента. Резултатите от представянето на изследваните изделия съответстват на тези, очаквани за този тип изделие, когато се използват по предназначение.

Потенциалните нежелани странични ефекти, свързани с употребата на FemoSeal™ VCS включват нежеланите събития, често съобщавани при алтернативните начини за затваряне на артериотомия, напр. кръвоизлив и хематом. Като цяло честотата на поява на нежелани събития, докладвани при използването на FemoSeal™ VCS, е подобна на честотата, докладвана при ръчна компресия и подобни изделия за съдово затваряне. По-конкретно, за кръвоизлив и хематом съобщените проценти за FemoSeal™ са по-ниски от съобщените проценти за подобни изделия за съдово затваряне. Всяко от докладваните нежелани



събития, както от публикуваната литература, така и от постмаркетинговото наблюдение, е било предварително идентифицирано (вж. **Раздел 1.3**).

Съществуващите данни относно клиничната безопасност и действието на FemoSeal™ VCS предполагат, че ползите за пациентите от използването на това изделие за затваряне на съдове надвишават евентуалните рискове, когато се използва в съответствие с инструкциите за употреба.

Както е посочено в предишните раздели по-горе, предоставените данни за FemoSeal™ VCS демонстрират съответствие между данните, свързани с оценяваното устройство (напр. използване на устройството, резултати по отношение на безопасността, клинична ефективност и клинични ползи) и идентифицирани еквивалентни устройства и данните, свързани с подобни устройства, посочени сред най-съвременните технологии.

Кръстосаният анализ на данните за безопасност не установи несъответствия между:

- Данните, посочени за най-съвременните технологии
- Данните, специфични за оценяваното устройство
- Данните, посочени във файла/файловете за управление на риска
- Данните, посочени на етикета и/или в инструкциите за употреба (т.е. адресирани са остатъчните рискове, които трябва да бъдат съобщени на потребителя).

Клиничната безопасност е доказана чрез нисък процент на усложнения, идентифицирани в публикуваната рецензирана клинична литература, спонсирани от компанията клинични проучвания, преглед на данните след пускане на пазара, съчетани с липса на изтегляне от пазара. Не са установени проблеми с ефективността, прегледаната литература съдържа използване на FemoSeal™ VCS, което е в съответствие с предназначението на производителя.

### **1.5 Възможни диагностични или терапевтични алтернативи**

Ръчната компресия традиционно се използва за постигане на хемостаза на мястото на артериотомия след съдови катетеризации. Ръчната компресия е свързана с обездвижване на пациента за дълги периоди от време (до 8 часа след процедурата) и със значителен дискомфорт и продължителен болничен престой. Наскоро проведен систематичен преглед установи, че средното време за постигане на хемостаза с ръчна компресия е 20,8 минути<sup>1</sup>.

Алтернативите на ръчната компресия включват външни хемостатични изделия, които прилагат механична компресия на мястото на артериотомията. Тези изделия не съкращават времето до хемостаза или времето до раздвижване, но намаляват изискванията за персонал чрез замяна на ръчната компресия с механична компресия. Честотата на нежеланите събития, свързани с използването на механична компресия, е подобна на честотата при ръчна компресия.



Устройствата за затваряне на съдове, като FemoSeal™ VCS, са проектирани да затворят артериотомията. Целта им е да намалят времето до хемостаза и да дадат възможност за по-ранно раздвижване. Наскоро проведен систематичен преглед, включващ 13 налични в търговската мрежа устройства, установи, че средното време за постигане на хемостаза с устройство за затваряне на съдове е 5.4 минути. Средното време до хемостаза за отделните изделия за затваряне на съдове варира от 1 минута (FemoSeal™ VCS) до 14 минути; като при повечето изделия е между 4 и 10 минути<sup>1</sup>.

Често съобщаваните нежелани събития, свързани със затваряне на мястото на артериотомия с ръчна компресия, външни хемостатични изделия или изделия за затваряне на съдове, включват хематом, кървене на мястото на достъп, псевдоаневризма, артериовенозна фистула и инфекция. Същият систематичен преглед (34 рандомизирани контролирани изпитвания, 14 401 пациенти) установи, че честотата на нежеланите събития е сходна между ръчната компресия и използването на изделия за затваряне на съдове, с изключение на това, че кървенето е склонно да бъде малко по-високо при изделията за затваряне на съдове<sup>1</sup>.

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Предложен потребителски профил и обучение

Целевите потребители на FemoSeal™ Vascular Closure System са лекари с обучение, което ги квалифицира да извършват артериален достъп и затваряне след ендоваскуларни процедури през общата феморална артерия и които са участвали в програмата за обучение на лекари на Terumo Medical Corporation за FemoSeal™.

## 1.7 Приложими хармонизирани и общи стандарти

| Справка за стандартите | Текуща година на съответствие/Ред. | Описание                                                                                             |
|------------------------|------------------------------------|------------------------------------------------------------------------------------------------------|
| ISO 11070              | 2014/AMD1:2018                     | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                  |
| EN ISO 11070           | 2014/A1:2018                       | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                  |
| FDA Guidance           | May 20, 2021                       | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment |

| Справка за стандартите | Текуща година на съответствие/Ред. | Описание                                                                                                                                                                 |
|------------------------|------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F2052             | 2015                               | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment                                 |
| ASTM F2213             | 2017                               | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment                                             |
| ASTM F2503             | 2020                               | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                                                           |
| ASTM F2182             | 2019                               | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging                                    |
| EN ISO 13485           | 2016/A11:2021                      | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 13485              | 2016                               | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 14644-1            | 2015                               | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1         | 2015                               | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2            | 2015                               | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2         | 2015                               | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3            | 2019                               | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |

| Справка за стандартите  | Текуща година на съответствие/Ред. | Описание                                                                                                                                      |
|-------------------------|------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 14644-3          | 2019                               | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                      |
| ISO 14698-1             | 2003                               | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                         |
| EN ISO 14698-1          | 2003                               | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                         |
| ISO 14698-2             | 2003/TC1:2004                      | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| EN ISO 14698-2          | 2003/TC 1:2004                     | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| USP <788>               | Не е приложимо                     | PARTICULATE MATTER IN INJECTIONS                                                                                                              |
| Фармакопея на EC 2.9.19 | Не е приложимо                     | Particulate Contamination: Sub-Visible Particles                                                                                              |
| IEC 62366-1             | 2015                               | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN 62366-1              | 2015                               | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN ISO 14971            | 2019/A11:2021                      | Medical devices — Application of risk management to Medical devices                                                                           |
| ISO 14971               | 2019                               | Medical devices — Application of risk management to Medical devices                                                                           |
| ASTM F1980              | 2016                               | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                                           |
| EN ISO 10993-1          | 2020                               | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                    |

| Справка за стандартите | Текуща година на съответствие/Ред. | Описание                                                                                                             |
|------------------------|------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| ISO 10993-1            | 2018                               | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2         | 2006                               | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2            | 2006                               | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3         | 2014                               | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3            | 2014                               | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4         | 2017                               | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4            | 2017                               | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| EN ISO 10993-5         | 2009                               | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| ISO 10993-5            | 2009                               | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| EN ISO 10993-6         | 2016                               | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |
| ISO 10993-6            | 2016                               | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |
| EN ISO 10993-10        | 2023 г.                            | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                       |
| ISO 10993-10           | 2021                               | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                       |
| EN ISO 10993-11        | 2018                               | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                      |

| Справка за стандартите | Текуща година на съответствие/Ред. | Описание                                                                                                                                   |
|------------------------|------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-11           | 2017                               | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| EN ISO 10993-12        | 2021                               | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| ISO 10993-12           | 2021                               | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| EN ISO 10993-17        | 2009                               | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17           | 2002 г.                            | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18           | 2020/A1:2022                       | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |
| EN ISO 10993-18        | 2020/A1:2022                       | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |
| EN ISO 10993-23        | 2021                               | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |
| ISO 10993-23           | 2021                               | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |
| ASTM F2382             | 2018                               | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)          |
| ASTM F756              | 2017                               | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                      |
| USP <85>               | Не е приложимо                     | [Bacterial Endotoxins Test. (Sterility)]                                                                                                   |

| Справка за стандартите | Текуща година на съответствие/Ред. | Описание                                                                                                                                                                     |
|------------------------|------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| USP <161>              | Не е приложимо                     | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72         | 2019                               | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135           | 2014/A1:2019                       | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135              | 2014/A1:2018                       | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7         | 2008/A1:2022                       | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |
| ISO 10993-7            | 2008/A1:2019                       | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                                            |
| EN 556-1               | 2024                               | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices              |
| EN ISO 11737-1         | 2018/A1:2021                       | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                                        |
| ISO 11737-1            | 2018/A1:2021                       | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                                        |
| EN ISO 11138-1         | 2017                               | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                                 |
| ISO 11138-1            | 2017                               | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                                 |

| Справка за стандартите | Текуща година на съответствие/Ред. | Описание                                                                                                                                 |
|------------------------|------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 11138-2         | 2017                               | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| ISO 11138-2            | 2017                               | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| EN ISO 15223-1         | 2016                               | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| ISO 15223-1            | 2016                               | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| EN 1041                | 2008/A1:2013                       | Information supplied by the manufacturer of medical devices                                                                              |
| EN ISO 11607-1         | 2020/A1:2023                       | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| ISO 11607-1            | 2019/A1:2023                       | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| EN ISO 11607-2         | 2020/A1:2023                       | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes       |
| ISO 11607-2            | 2019/A1:2023                       | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes       |
| ASTM D4169             | 2016                               | Standard Practice for Performance Testing of Shipping Containers and Systems                                                             |
| ASTM F1886/F1886M      | 2016                               | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                      |

| Справка за стандартите | Текуща година на съответствие/Ред. | Описание                                                                                                                                                                           |
|------------------------|------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F2825             | 2018                               | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                           |
| ASTM F2096             | 2011 (R 2019)                      | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                                       |
| ASTM F88/F88M          | 2015                               | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                               |
| MDCG 2021- 24          | 2021                               | Guidance on classification of medical devices                                                                                                                                      |
| MDCG 2020- 3           | 2020                               | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD         |
| MDCG 2020- 8           | 2020                               | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                                     |
| MDCG 2020-7            | 2020                               | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                                  |
| MDCG 2020- 6           | 2020                               | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                               |
| MDCG 2019-9 v1         | 2022                               | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                           |
| MDCG 2019-8 v2         | 2020                               | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices |
| MDCG 2020- 15          | 2020                               | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                           |
| MDCG 2021- 11          | 2021                               | Guidance on Implant Card – ‘Device types’                                                                                                                                          |



| Справка за стандартите | Текуща година на съответствие/Ред. | Описание                                                                                                                                                                                                                                                      |
|------------------------|------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2021- 19          | 2021                               | Guidance note integration of the UDI within an organisation's quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4         | 2021                               | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2            | 2019                               | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019- 1           | 2019                               | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018- 7           | 2018                               | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018- 6           | 2018                               | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |
| MDCG 2018- 4           | 2018                               | MDCG 2018-4 Annex: UDI database Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                                                                                                  |
| MDCG 2018-3 v1         | 2020                               | Guidance on UDI for systems and procedure packs                                                                                                                                                                                                               |
| MDCG 2021- 25          | 2021                               | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC                                                                 |
| Meddev 2.12-2 Rev 2    | 2012                               | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                                                                                        |

## 2.0 БИБЛИОГРАФИЯ

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### 3.0 ИСТОРИЯ НА ВЕРСИИТЕ

| Номер на редакцията на SSCP | Дата на издаване  | Описание на промените                                                | Редакция, валидирана от нотифицирания орган                                                                                                                                                                                                                                                                                            |
|-----------------------------|-------------------|----------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022                | 20 януари 2023 г. | Първоначална публикация, при сертифициране от MDR CE                 | <p><input checked="" type="checkbox"/> Да</p> <p>Език на валидиране: English</p> <p><input type="checkbox"/> Не (приложимо само за имплантируеми устройства от клас IIa или IIb (MDR, член 52 (4), 2-ри параграф), за които SSCP все още не е валидирано от нотифицирания орган)</p> <p><input type="checkbox"/> Друго (уточнете):</p> |
| SSCP-FS-2023 – Редакция 1   | 15 март 2024 г.   | Актуализирано за периода от 1 януари 2019 г. до 31 декември 2023 г.  | <p><input checked="" type="checkbox"/> Да</p> <p>Език на валидиране: English</p> <p><input type="checkbox"/> Не (приложимо само за имплантируеми устройства от клас IIa или IIb (MDR, член 52 (4), 2-ри параграф), за които SSCP все още не е валидирано от нотифицирания орган)</p> <p><input type="checkbox"/> Друго (уточнете):</p> |
| SSCP-FS-2024<br>1 издание   |                   | Актуализирано за периода от 1 септември 2019 г. до 31 август 2024 г. | <p><input type="checkbox"/> Да</p> <p>Език на валидиране: English</p> <p><input type="checkbox"/> Не (приложимо само за имплантируеми устройства от клас IIa или IIb (MDR, член 52 (4), 2-ри параграф), за които SSCP все още не е</p>                                                                                                 |

|                           |               |                                                                     |                                                                                                                                                                                                                                                                                                                                                  |
|---------------------------|---------------|---------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                           |               |                                                                     | валидирано от<br>нотифицирания орган)<br><br><input type="checkbox"/> Друго (уточнете):                                                                                                                                                                                                                                                          |
| SSCP-FS-2024<br>2 издание | June 20, 2025 | Преработено въз<br>основа на запитвания<br>на НСАИ за<br>валидиране | <input checked="" type="checkbox"/> Да<br>Език на валидиране:<br>English<br><br><input type="checkbox"/> Не (приложимо само за<br>имплантируеми устройства от<br>клас IIa или IIb (MDR, член<br>52 (4), 2-ри параграф), за<br>които SSCP все още не е<br>валидирано от<br>нотифицирания орган)<br><br><input type="checkbox"/> Друго (уточнете): |

**Souhrn údajů o bezpečnosti a klinické funkci**  
**Systém FemoSeal™ Vascular Closure System**

|                                                      |                                                                                             |
|------------------------------------------------------|---------------------------------------------------------------------------------------------|
| <b>Výrobce</b>                                       | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 USA         |
| <b>SRN výrobce</b>                                   | US-MF-000019594                                                                             |
| <b>Zástupce vedení / PRRC</b>                        | Kimberly Feitl<br>Vicepresident, oddělení kvality                                           |
| <b>Základní UDI-DI</b>                               | 38970FS79                                                                                   |
| <b>Kód EMDN</b>                                      | C900199 – Systémy hemostázy – Jiné                                                          |
| <b>Třída prostředku</b>                              | Třída III                                                                                   |
| <b>Rok, kdy prostředek poprvé získal označení CE</b> | 2005                                                                                        |
| <b>Zástupce v EU</b>                                 | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgie<br>SRN: BE-AR-000001433 |
| <b>Oznámený subjekt</b>                              | NSAI<br>CE 0050                                                                             |

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Cílem tohoto souhrnu údajů o bezpečnosti a klinické funkci (SSCP) je zajistit veřejný přístup k aktualizovanému souhrnu hlavních aspektů bezpečnosti a klinické funkce systému na uzavírání cév FemoSeal™ Vascular Closure System (VCS).

Souhrn údajů o bezpečnosti a klinické funkci prostředku určený pro uživatele / zdravotnické pracovníky je uveden níže v **části 1.0**.

## **1.0 SOUHRN PRO UŽIVATELE / ZDRAVOTNICKÉ PRACOVNÍKY**

SSCP není určen jako náhrada návodu k použití, který je hlavním dokumentem k zajištění bezpečného používání prostředku, ani není určen k poskytování doporučení týkajících se diagnostiky nebo léčby určeným uživatelům nebo pacientům. Cílem SSCP není nahradit povinné údaje na kartě s informacemi o implantátu ani v žádných jiných povinných dokumentech.

### **1.1 Určené použití prostředku**

#### **1.1.1 Určené použití**

Systém FemoSeal™ Vascular Closure System je zdravotnický prostředek určený k uzavření arteriální punkce po perkutánní katetrizaci přes společnou femorální tepnu.

#### **1.1.2 Indikace pro použití**

Systém FemoSeal™ Vascular Closure System je indikován k použití při uzavírání punkce společné femorální tepny (arteriotomie) u pacientů, kteří podstoupili perkutánní katetrizaci pomocí zavaděče velikosti 7F (2,33 mm) nebo menšího.

#### **1.1.3 Kontraindikace a/nebo omezení**

Systém FemoSeal™ Vascular Closure System je kontraindikován u pacientů s arteriotomiemi, u nichž byly použity zavaděče nebo prostředky větší než 7F (2,33 mm).

#### **1.1.4 Cílové populace pacientů**

Bezpečnost a účinnost systému FemoSeal™ Vascular Closure System byla stanovena u pacientů starších 18 let, kteří podstoupili perkutánní katetrizaci s použitím zavaděče velikosti 7F (2,33 mm) nebo menšího.

#### **1.1.5 Zvláštní populace pacientů**

Bezpečnost a účinnost systému FemoSeal™ Vascular Closure System nebyla stanovena u následujících populací pacientů:

- pacienti s již existujícím autoimunitním onemocněním,
- pacienti podstupující terapeutickou trombolýzu,
- pacienti s klinicky významným periferním cévním onemocněním,
- pacienti s nekontrolovanou hypertenzí (> 220 mmHg u systolického tlaku nebo > 110 mmHg u diastolického tlaku),
- pacienti s krvácivou poruchou, včetně trombocytopenie (počet trombocytů < 100 000) nebo anémie (Hgb < 10 mg/dl),

- pacienti s vnitřním lumenem společné femorální tepny menším než 5 mm,
- pacienti s poruchou funkce ledvin a/nebo jater,
- pacienti s jinou relevantní komorbiditou,
- populace s určitým rasovým a/nebo etnickým původem,
- pacienti s infarktem myokardu během 72 hodin,
- pacienti s cévním štěpem nebo stentem v místě vpichu,
- pacientky, které jsou těhotné nebo kojí,
- pacienti mladší 18 let.

### 1.1.6 Určení uživatelé

Určenými uživateli systému FemoSeal™ Vascular Closure System jsou lékaři, kteří jsou vyškoleni v oblasti vytváření a uzavírání arteriálního přístupu k provádění endovaskulárních výkonů přes společnou femorální tepnu a absolvovali školicí program pro lékaře o prostředku FemoSeal™ společnosti Terumo Medical Corporation.

## 1.2 Popis prostředku

### 1.2.1 Popis prostředku

Systém FemoSeal™ Vascular Closure System, který vyrábí společnost Terumo Medical Corporation (TMC), je vstřebatelný prostředek na uzavírání cév určený k dosažení hemostázy po perkutánní katetrizaci přes společnou femorální tepnu.

Uzavírací prvky systému FemoSeal™ se skládají ze dvou vstřebatelných polymerních disků, vnitřního uzavíracího a vnějšího zamykacího disku, které jsou spojeny vstřebatelným pleteným vláknem a tím mechanicky utěšňují arteriotomii (viz **obrázek 1.1** a **obrázek 1.2**). Po umístění přes zavaděč s kuželovitým pouzdem se vnější zamykací disk přitlačí na dřík z pleteného vlákna, čímž dojde k mechanickému uzavření místa vpichu mezi vnitřním a vnějším zamykacím diskem. Vnitřní uzavírací a vnější zamykací disk drží na místě třením o dřík z pleteného vlákna. Hemostázy je dosaženo mechanickými prostředky. Uzavírací prvky se rozkládají hydrolyzou.

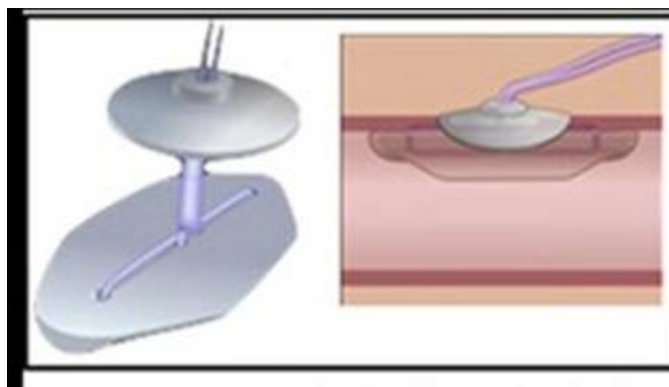
Implantovatelné uzavírací součásti, vnitřní uzavírací a vnější zamykací disk, se rozloží za osmnáct (18) měsíců, zatímco u pleteného vlákna se odhaduje, že rozklad a vstřebání hydrolyzou okolní tkáně nastane po dvou (2) až třech (3) letech. Schopnost implantovatelných uzavíracích součástí udržovat kompresi arteriotomie byla testována po dobu až osmi (8) hodin. Produkty rozkladu jsou metabolizovány a vylučovány močí nebo ve formě oxidu uhličitého vydechovány plícemi. Ve studiích na zvířatech nebyly pozorovány žádné kumulativní účinky. Dalšími součástmi systému

FemoSeal™, které se během výkonu dostanou do styku s živou tkání nebo krví, jsou zavaděč s kuželovitým pouzdem, dilatátor, přechovací trubice, zasunovací prvek a vodící drát.

**Obrázek 1.1 Vnitřní uzavírací disk a vnější zamykací disk**

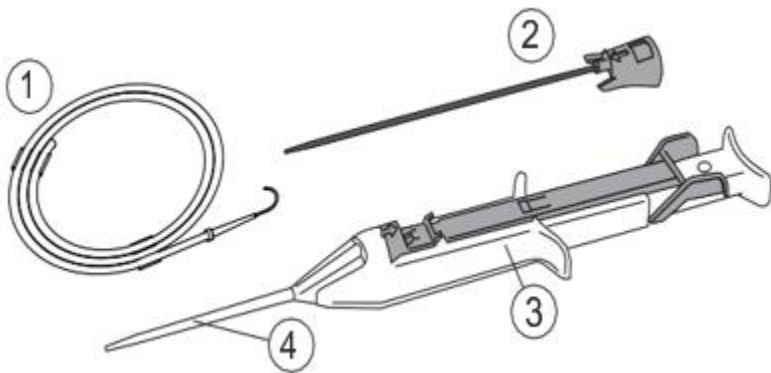


**Obrázek 1.2 Umístění vnitřního uzavíracího a vnějšího zamykacího disku**



Jednotka FemoSeal™ je balena společně s dilatátorem a vodícím drátem o délce 70 cm (27,5") s vnějším průměrem 0,97 mm (0,038") a s vyrovnávačem ve tvaru J, viz **obrázek 1.3** níže. Vodicí drát je uzavřen v polyetylenové hadičce. Všechny součásti jsou zabaleny na pevné papírové podložce. Balení obsahuje také kartu s informacemi o implantátu pacienta. Systém FemoSeal™ Vascular Closure System nevyžaduje další příslušenství, aby mohl fungovat tak, jak má, a je určen pouze pro použití s dilatátorem a vodícím drátem, které jsou součástí balení výrobku.

Obrázek 1.3 Jednotka systému FemoSeal™ VCS s vodicím drátem a dilatátorem



### 1.2.2 Suroviny a součásti

V **tabulce 1.1** níže jsou uvedeny součásti systému FemoSeal™ VCS.

**Tabulka 1.1 Suroviny a součásti systému FemoSeal™ VCS**

| Číslo součásti | Popis                                                                 |                                                          | Materiály                                                                                                                                                                  |
|----------------|-----------------------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1              | Vodicí drát 0,97 mm (0,038") s vyrovnávačem vodicího drátu ve tvaru J |                                                          | Vodicí drát: Nerezová ocel 304<br><br>Vyrovnávač vodicího drátu ve tvaru J: Polypropylen, purpurový pigment<br><br>Svorka: polyetylen<br><br>Hadička: polyetylen           |
| 2              | Dilatátor FemoSeal                                                    |                                                          | Hrdlo: tetrahydrofuran, modrý pigment, polybutylentereftalát (PBT)<br><br>Hadička: vysokohustotní polyetylen (HDPE), černý pigment<br><br>Mazivo: Silicone Dow Corning 360 |
| 3/4            | Jednotka FemoSeal                                                     | Lisovaný RD7 – vnitřní uzavírací a vnější zamykací disk* | Kopolymer glykolidu, trimethylenkarbonátu, ε-kaprolaktonu a TMP: trimethylolpropanu (iniciátor)                                                                            |
|                |                                                                       | Pletené vlákno*                                          | Segmentovaný kopolymer L,L-laktidu, trimethylenkarbonátu, ε-kaprolaktonu a 1,3 propandiolu (iniciátor)                                                                     |

|  |  |                               |                                                         |
|--|--|-------------------------------|---------------------------------------------------------|
|  |  |                               | Potah je kopolymer glykolidu, ε-kaprolaktonu a L-lysinu |
|  |  | Pěchovací trubice             | Polypropylen                                            |
|  |  | Zasunovací prvek              | Nerezová ocel 304V                                      |
|  |  | Posuvník                      | Polybutylentereftalát (PBT)                             |
|  |  | Pouzdro                       | Polybutylentereftalát (PBT)                             |
|  |  | Tlačítko                      | Polybutylentereftalát (PBT)                             |
|  |  | Kryt tlačítka                 | Polyoxymethylen (POM) / polyacetalový kopolymer         |
|  |  | Objímka                       | Polybutylentereftalát (PBT)                             |
|  |  | Rozpěrka                      | Polybutylentereftalát (PBT)                             |
|  |  | Kužel                         | Polypropylen                                            |
|  |  | Víko pouzdra                  | Polybutylentereftalát (PBT)                             |
|  |  | Bezpečnostní západka          | Polybutylentereftalát (PBT), modrý pigment              |
|  |  | Kryt objímky                  | Polybutylentereftalát (PBT)                             |
|  |  | Těsnění trubice               | Silikon, Shore A 70                                     |
|  |  | Těsnění pouzdra               | Silikon, Shore A 50                                     |
|  |  | Pružina                       | Nerezová ocel 302                                       |
|  |  | Zavaděč s kuželovitým pouzdem | Polypropylen<br>Silikon Dow Corning 360, hexan          |

\*Implantovatelná část prostředku; implantovatelné součásti jsou bezpečné při MR

Systém FemoSeal™ VCS je sterilizován etylenoxidem (EO) a je to zdravotnický prostředek pro jedno použití. Systém FemoSeal™ VCS je navržen tak, aby jej nebylo možné použít znovu.

### **Způsob účinku**

Systém FemoSeal™ VCS podporuje mechanickou hemostázu umístěním implantovatelných uzavíracích prvků uvnitř a vně společné femorální tepny. Mechanismus, který zabraňuje krvácení, zajišťuje vnitřní uzavírací disk, který utěsňuje místo vpichu, a vnější zamykací disk, který drží vnitřní uzavírací disk na místě.

### **1.2.3 Klinický přínos**

Systém FemoSeal™ VCS poskytuje v souvislosti s uzavřením cévy po punkci společné femorální tepny následující klinické přínosy:

- Zkrácení doby do dosažení hemostázy<sup>1</sup>
- Zkrácení doby do mobilizace pacienta<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

#### 1.2.4 Předchozí generace nebo varianty

- První verze systému FemoSeal™ VCS (č. 11200) se prodávala na evropském trhu v průběhu roku 2005 a po část roku 2006.
- Současný systém FemoSeal™ VCS (č. 11202) s vylepšeným zaváděcím systémem je na trhu od 28. března 2006.

#### 1.2.5 Příslušenství určené k použití v kombinaci s prostředkem

Jednotka FemoSeal™ je balena společně s dilatátorem, vodicím drátem o délce 70 cm (27,5") s vnějším průměrem 0,97 mm (0,038") a s vyrovnávačem ve tvaru J. Vodicí drát je příslušenstvím jednotky FemoSeal™. Vyrovnávač ve tvaru J je součástí vodicího drátu, zatímco dilatátor je součástí jednotky FemoSeal™. Vodicí drát je jediným vhodným příslušenstvím. Vodicí drát je uzavřen v polyetylenové hadičce. Všechny součásti jsou zabaleny na pevné papírové podložce. Balení obsahuje také kartu s informacemi o implantátu pacienta. Systém FemoSeal™ Vascular Closure System nevyžaduje další příslušenství, aby mohl fungovat tak, jak má, a je určen pouze pro použití s dilatátorem a vodicím drátem, které jsou součástí balení výrobku.

#### 1.2.6 Další prostředky a výrobky určené k použití v kombinaci s prostředkem

Systém FemoSeal™ VCS nevyžaduje k tomu, aby mohl fungovat tak, jak má, žádné další prostředky.

### 1.3 Rizika a výstrahy

#### 1.3.1 Zbytková rizika a nežádoucí účinky

Známé nebo předvídatelné nežádoucí příhody, poškození a komplikace spojené s použitím prostředku FemoSeal™ VCS v důsledku zbytkových rizik jsou uvedeny v **tabulce 1.2**. Četnost výskytu je založena na analýze dokumentace rizik a vypočítávána na základě údajů ze sledování po uvedení na trh od 1. září 2019 do 31. srpna 2024. Pro systém FemoSeal™ VCS nejsou známa žádná zbytková rizika a všechna příslušná rizika byla řešena prostřednictvím návodu k použití a procesu řízení rizik.



**Tabulka 1.2. Nežádoucí příhody / komplikace spojené s prostředkem FemoSeal**

| Újma                                   | Frekvence výskytu (%) | Zmírňující faktory                                                                                                                                           |
|----------------------------------------|-----------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Alergická reakce                       | 0,0000                | Opatření a plány na maximální možné snížení rizika vycházejí z konstrukčních charakteristik výrobku, pokynů pro výrobu, označování výrobků a školení lékařů. |
| Aneuryzma                              | 0,0000                |                                                                                                                                                              |
| AV píštěl                              | 0,0001                |                                                                                                                                                              |
| Ztráta krve / krvácení                 | 0,0280                |                                                                                                                                                              |
| Smrt                                   | 0,0002                |                                                                                                                                                              |
| Ekchymóza                              | 0,0000                |                                                                                                                                                              |
| Embolizace                             | 0,0000                |                                                                                                                                                              |
| Reakce na cizí těleso                  | 0,0000                |                                                                                                                                                              |
| Hematom                                | 0,0027                |                                                                                                                                                              |
| Krvácení                               | 0,0001                |                                                                                                                                                              |
| Infekce                                | 0,0002                |                                                                                                                                                              |
| Zánětlivá reakce                       | 0,0000                |                                                                                                                                                              |
| Necitlivost                            | 0,0000                |                                                                                                                                                              |
| Bolest                                 | 0,0000                |                                                                                                                                                              |
| Pocit nepohody pacienta                | 0,0004                |                                                                                                                                                              |
| Prodleva při zákroku                   | 0,0065                |                                                                                                                                                              |
| Pseudoaneuryzma                        | 0,0004                |                                                                                                                                                              |
| Retroperitoneální krvácení             | 0,0002                |                                                                                                                                                              |
| Sepse                                  | 0,0000                |                                                                                                                                                              |
| Tromboembolie                          | 0,0000                |                                                                                                                                                              |
| Trombóza                               | 0,0001                |                                                                                                                                                              |
| Okluze cévy / ischemie dolní končetiny | 0,0002                |                                                                                                                                                              |
| Perforace cévy                         | 0,0000                |                                                                                                                                                              |
| Disekce /lacerace cévní tkáně          | 0,0003                |                                                                                                                                                              |

### 1.3.2 Výstrahy a preventivní opatření

#### Výstrahy

1. Prostředek nepoužívejte, pokud je poškozen jeho obal nebo pokud je porušená některá ze sterilních bariér.
2. Prostředek nepoužívejte po uplynutí data expirace – biologicky rozložitelné součásti nemusí být dostatečně funkční.
3. Prostředek nepoužívejte, pokud se některé jeho součásti zdají být poškozené nebo vadné.
4. Použití systému FemoSeal™ Vascular Closure System v případech, kdy mohlo dojít k bakteriální kontaminaci zavaděče nebo okolní tkáně, může způsobit infekci.
5. Pokud existuje podezření, že došlo k punkci zadní arteriální stěny, nebo byla provedena více než jedna arteriální punkce, nespolehejte při zajišťování arteriální hemostázy výhradně na systém FemoSeal™ Vascular Closure System. Použijte dodatečnou manuální nebo mechanickou kompresi.
6. Pokud se místo vpichu nachází v oblasti bifurkace společné femorální tepny nebo distálně od ní, systém FemoSeal™ Vascular Closure System se nemá použít, protože by hrozilo riziko nesprávného umístění uzavíracího disku. To by mohlo vést ke krvácivým komplikacím a/nebo k narušení normálního průtoku krve.
7. Pokud dochází k přetrvávajícímu arteriálnímu krvácení z místa incize, neodřezávejte pletené vlákno, dokud nebude dosaženo hemostázy. Pokud není dosaženo hemostázy, připevněte pletené vlákno sterilním krytím na rány a proveďte dodatečnou kompresi, dokud nebude dosaženo hemostázy. V případě přetrvávajícího arteriálního krvácení mohou nastat závažné krvácivé komplikace, které mohou vést k poranění nebo smrti pacienta.
8. Nepoužívejte systém FemoSeal™ Vascular Closure System, pokud se místo vpichu nachází proximálně od tříselného vazů, protože by to mohlo způsobit retroperitoneální hematom.
9. Pacienti s vyšším rizikem krvácení mohou utrpět zvýšenou ztrátu krve vyžadující transfuzi.
10. Pokud se uvolní uzavírací disk, může potenciálně způsobit trombotickou a/nebo embolickou příhodu.

#### Preventivní opatření

1. Zárok zavedení systému FemoSeal™ Vascular Closure System by měli provádět lékaři s odpovídajícím školením v používání prostředku.

2. Před zavedením systému FemoSeal™ Vascular Closure System proveďte zjednodušený femorální angiogram nebo ultrazvukem naváděnou femorální punkci.
3. V následujících případech zákrok přerušte:
  - průměr lumen společné femorální tepny < 5 mm,
  - přítomnost stenózy a/nebo významného plaku v blízkosti místa punkce společné femorální tepny,
  - arteriální punkce se nachází v místě bifurkace femorální tepny nebo distálně k němu,
  - přítomnost anomálních větví nebo cévních abnormalit v blízkosti místa punkce společné femorální tepny.
4. Pokud je přítomen hematoma, je třeba věnovat zvláštní pozornost správnému zavedení zavaděče s kuželovitým pouzdrům do tepny.
5. Použijte techniku punkce jedné stěny. Nepropíchněte zadní stěnu tepny.
6. Při používání systému FemoSeal™ Vascular Closure System stále dodržujte sterilitu postupy.
7. Systém FemoSeal™ Vascular Closure System je určen pouze k jednorázovému použití a nesmí se v žádném případě opakovaně sterilizovat ani opakovaně používat. Jednotka FemoSeal™ je navržena tak, aby ji nebylo možné použít znovu.
8. Pokud se při zavádění vnitřního uzavíracího disku setkáte s neočekávaným odporem, zákrok přerušte.
9. Pro správné umístění vnitřního uzavíracího disku přesuňte palec tak, aby se tlačítko mohlo volně vrátit do původní polohy.
10. Před umístěním vnějšího zamykacího disku se ujistěte, zda je hrot zavaděče s kuželovitým pouzdrům jednotky FemoSeal™ pod povrchem kůže. U pacientů s krátkou vzdáleností mezi společnou femorální tepnou a úrovní kůže může být vnější zamykací disk neúmyslně umístěn nad úroveň kůže.
11. Aby bylo možné provést umístění správně, může být před umístěním nutné provést incizi kůže.
12. Pokud je vnitřní uzavírací disk uvnitř tepny, ale není možné zcela stisknout tlačítko a umístit vnější zamykací disk, může být nutné prvky uzavíracího systému FemoSeal™ chirurgicky odstranit.
13. Pokud je potřeba během 18 měsíců provést opětovnou punkci stejné společné femorální tepny, je nutné opětovnou punkci provést nejméně jeden centimetr proximálně od předchozího místa přístupu systému FemoSeal™ Vascular Closure System.

14. Poučte pacienta, aby dodržoval pokyny lékaře týkající se kontroly místa uzavření.

15. Poučte pacienta, aby po dobu následujících 18 měsíců u sebe nosil informační kartu pacienta.

### **Preventivní opatření v době propuštění**

Dříve než budete zvažovat propuštění pacienta, proveďte u něj posouzení následujících klinických stavů:

1. krvácení a/nebo hematom v místě uzavření,
2. bolest při chůzi,
3. známky infekce v místě uzavření.

### **1.3.3 Bezpečnostní nápravná opatření v terénu**

Jedno bezpečnostní nápravné opatření v terénu týkající se systému FemoSeal™ VCS bylo provedeno v období od 1. září 2019 do 31. srpna 2024.

V roce 2022 společnost Terumo dobrovolně stáhla systém FemoSeal™ VCS z důvodu stížností na selhání při testování procesu a uvolnění šarže prostředku FemoSeal pro měření přechovací síly a retrakční síly vyrobeného společností Elkton. Z Jižní Koreje bylo staženo celkem 950 jednotek.

## **1.4 Klinické hodnocení a následné klinické sledování po uvedení na trh**

**Tabulka 1.3** obsahuje seznam hlavních studií provedených za účelem uvedení systému FemoSeal™ VCS na trh, jakož i studií a následných klinických činností po uvedení na trh.

V tabulce níže je uvedena i verze prostředku použitého ve studii. První verze systému FemoSeal™ VCS (č. 11200) byla na trhu do roku 2006, přičemž další verze (č. C11202) byla na trh uvedena v roce 2006 a je to verze, která je na trhu i v současnosti.

**Tabulka 1.3 Souhrn hlavních studií**

| <b>Zkoušky funkčnosti na zvířatech před uvedením na trh</b>                                                                                                                                                                                                             | <b>Verze prostředku</b> |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                   |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                   |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                   |

| <b>První klinická studie u člověka</b>                                                                                                                                                                       |                                 |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 11200                           |
| <b>Realizované klinické studie po uvedení na trh</b>                                                                                                                                                         |                                 |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                   | C11202<br>(současný prostředek) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                            | C11202<br>(současný prostředek) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                                                                                               | C11202<br>(současný prostředek) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)                                                                                       | C11202<br>(současný prostředek) |
| <b>Plánované / probíhající klinické studie po uvedení na trh</b>                                                                                                                                             |                                 |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                                                                                                   | C11202<br>(současný prostředek) |
| <b>Následné klinické činnosti po uvedení na trh</b>                                                                                                                                                          |                                 |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                                                                                                    | C11202<br>(současný prostředek) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                                                                                                           | C11202<br>(současný prostředek) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024)                                                                              | C11202<br>(současný prostředek) |

#### 1.4.1 Souhrn údajů před uvedením na trh (testování na zvířatech a klinická hodnocení)

**Tabulka 1.4** níže popisuje všechny studie před uvedením na trh, a to jak na testování na zvířatech, tak klinická hodnocení.

**Tabulka 1.4 Souhrny studií před uvedením na trh**

| Zkoušky funkčnosti na zvířatech před uvedením na trh                                                                                                                                                                                                                    |                                                                              |                                        |                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
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| Název studie                                                                                                                                                                                                                                                            | Rok / hlavní zkoušející                                                      | Typ studie                             | Cíle                                                                                                                                                                                                                                     | Milníky                                                                                                                                                                                                                                                                                                                                                                                                                                  | Potenciální kritéria přijatelnosti                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 2000<br>Radi Medical System AB<br><br>Provedla společnost Biomatech, Francie | Studie na zvířatech; průzkumné šetření | Cílem studie bylo vyhodnotit biokompatibilitu a biologickou funkčnost biologicky rozložitelného implantátu určeného k dosažení hemostázy v cévním systému. Zpráva se zaměřuje na rezervní zvířata ze studie č. 862 (dokument č. 1051-01) | <p>N = 3 dospělé ovčí samice, 1 zvíře na jeden časový bod</p> <p>Sledování za účelem provedení histopatologické analýzy, makroskopické klasifikace a ultrastrukturální analýzy</p> <ul style="list-style-type: none"> <li>12 měsíců</li> <li>15 měsíců</li> <li>18 měsíců</li> </ul> <p>Sledování na základě barevného dopplerovského ultrazvukového vyšetření po dobu 30 dnů v místě karotidy a v místě přístupu do femorální tepny</p> | <p>Průchodnost tepny</p> <ul style="list-style-type: none"> <li>Hodnocení průtoku krve po zavedení – snížení průtoku krve o 2/3 spojené s dočasným arteriálním vazospasmem, který byl přičítán zákroku, v obou případech na levé společné femorální tepně</li> <li>Barevné dopplerovské ultrazvukové vyšetření (4 týdny) – 3/3 (100 %) bez výrazného snížení průtoku krve 30 dní po implantaci</li> </ul> <p>Makroskopická pozorování</p> <ul style="list-style-type: none"> <li>12 měsíců – průchodnost potvrzena makroskopicky absencí anatomicky viditelné okluze; nebyly zaznamenány žádné makroskopické lokální léze intolerance (krvácení, nekróza nebo neovaskularizace); zapouzdření vnitřního disku se zdálo být výrazné</li> <li>15 měsíců – při makroskopickém pozorování nebyly zjištěny žádné známky zánětu; nebyly identifikovány žádné zbytky vnitřního ani vnějšího disku; tkáň zapouzdření v oblasti vnějšího disku vypadala stejně jako při pozorování po 12 měsících</li> <li>18 měsíců – při makroskopickém pozorování nebyly zjištěny žádné známky lokální intolerance, vnější disk viditelný (3/3 případů), rozklad vnitřního disku dokončen, 1/3 (levá společná karotida) – deprese stěny tepny pozorovaná v místě implantátu (mohlo by</li> </ul> |

|                                                                                                                                                                                                                                                                                |                                                                                  |                                               |                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
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|                                                                                                                                                                                                                                                                                |                                                                                  |                                               |                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                          | <p>souviset s umístěním prostředku)</p> <p><b>Závěry</b></p> <ul style="list-style-type: none"> <li>• Z makroskopického hlediska nebyly 12, 15 a 18 měsíců po implantaci zjištěny žádné známky nekrózy, degenerace ani trombózy.</li> <li>• Zdálo se, že proces rozkladu vnitřního a vnějšího disku probíhá mezi 12. a 18. měsícem a v 18 měsících je dokončen, přičemž oblast implantace pokrývala bělavá tkáň.</li> <li>• Z histologického hlediska nebyl po 18 měsících již vidět polymerní materiál, ale byla přítomna endoluminální fibrózní tkáň. Nebyly zaznamenány žádné nekrotické, degenerativní ani trombotické léze.</li> </ul>                                         |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002 Radi Medical System AB</p> <p>Provedla společnost Biomatech, Francie</p> | <p>Studie na zvířatech; průzkumné šetření</p> | <p>Cílem studie bylo vyhodnotit biokompatibilitu biologicky rozložitelného implantátu určeného k dosažení hemostázy v cévním systému.</p> | <p>Následné sledování (po implantaci)</p> <ul style="list-style-type: none"> <li>• 12 týdnů</li> <li>• 24 týdnů</li> <li>• 36 týdnů</li> </ul> <p>N = 12 ovcí, 3 zvířata na jeden časový bod, 3 rezervní zvířata utracená ve 12, 15 a 18 měsících</p> <p>Místa implantace – pravá a levá femorální tepna, pravá a levá společná karotida</p> <p>Analýza na základě barevného dopplerovského ultrazvukového vyšetření</p> | <p><u>Průchodnost karotid a femorálních tepen po 4 týdnech</u></p> <ul style="list-style-type: none"> <li>• Významné snížení průtoku krve 0/12 (0 %)</li> </ul> <p><u>Žádné významné snížení průtoku krve</u></p> <ul style="list-style-type: none"> <li>• Závažné zhoršení průtoku krve v souvislosti se zavedením prostředku 0/12 (0 %)</li> <li>• Snížení průtoku krve v levé společné karotidě 2/12 (16,6 %) v důsledku dočasného arteriálního vazospasmu (připisovaného chirurgickému zákroku, nikoli prostředku)</li> </ul> <p><u>Snížení průtoku krve při následném sledování</u></p> <p>12 týdnů – 0/12 (0 %)</p> <p>24 týdnů – 0/12 (0 %)</p> <p>36 týdnů – 0/12 (0 %)</p> |

|  |  |  |  |  | <p>Měření krevního tlaku<br/>(3 ovce – 36 týdnů)</p> <ul style="list-style-type: none"> <li>Nebylo zjištěno žádné významné snížení průtoku krve</li> </ul> <p>Makroskopická data k integraci a rozkladu (třída 0–4)</p> <p><u>Místa na karotidě</u></p> <p><i>Vnitřní strana</i></p> <p>– zapouzdření</p> <p>12 týdnů 1,3</p> <p>24 týdnů 0,8</p> <p>36 týdnů 0,7</p> <p>– rozklad materiálu</p> <p>12 týdnů 2,2</p> <p>24 týdnů 2,3</p> <p>36 týdnů 0,7</p> <p><i>Vnější strana</i></p> <p>– zapouzdření</p> <p>12 týdnů 2,0</p> <p>24 týdnů 1,0</p> <p>36 týdnů 0,8</p> <p>– rozklad materiálu</p> <p>12 týdnů 2,0</p> <p>24 týdnů 2,7</p> <p>36 týdnů 3,2</p> <p><u>Místa na femorální tepně</u></p> <p><i>Vnější strana</i></p> <p>– zapouzdření</p> <p>12 týdnů 1,0</p> <p>24 týdnů 2,7</p> <p>36 týdnů 1,0</p> <p>– rozklad materiálu</p> <p>12 týdnů 2,0</p> <p>24 týdnů 2,4</p> <p>36 týdnů 3,0</p> <p><i>Vnitřní strana</i></p> <p>– zapouzdření</p> <p>12 týdnů 2,0</p> <p>24 týdnů 1,2</p> <p>36 týdnů 1,0</p> <p>– rozklad materiálu</p> <p>12 týdnů 1,0</p> <p>24 týdnů 2,2</p> <p>36 týdnů 3,0</p> |
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|  |  |  |  |  | <p><u>Histologické údaje k integraci, rozkladu a zánětlivým parametrům (průměr příslušných hodnot, index 0–4) n = 6</u></p> <p><u>Místa na karotidě</u></p> <p>Vnější fibróza<br/>12 týdnů – 2,3<br/>24 týdnů – 2,3<br/>36 týdnů – 1,8</p> <p>Vnitřní neointima<br/>12 týdnů – 3,0<br/>24 týdnů – 2,7<br/>36 týdnů – 3,3</p> <p>Rozklad materiálu<br/>12 týdnů – 1,7<br/>24 týdnů – 3,0<br/>36 týdnů – 3+</p> <p>Zánětlivé parametry (makrofágy)<br/>12 týdnů – 3,0<br/>24 týdnů – 1,7<br/>36 týdnů – 1,7</p> <p><u>Místa na femorální tepně</u></p> <p>Vnější fibróza<br/>12 týdnů – 1,3<br/>24 týdnů – 1,5<br/>36 týdnů – 1,7</p> <p>Vnitřní neointima<br/>12 týdnů – 3,7<br/>24 týdnů – 3,3<br/>36 týdnů – 3,8</p> <p>Rozklad materiálu<br/>12 týdnů – 2,0<br/>24 týdnů – 3,0<br/>36 týdnů – 3+</p> <p>Zánětlivé parametry (makrofágy)<br/>12 týdnů – 3,5<br/>24 týdnů – 1,8<br/>36 týdnů – 1,8</p> <p><u>Histomorfologické hodnoty průchodnosti</u></p> <p>Místa na karotidě<br/>12 týdnů 74,0 %<br/>24 týdnů 81,9 %<br/>36 týdnů – 89,43 %</p> <p>Místa na femorální tepně<br/>12 týdnů – 42,2 %</p> |
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|                                                                                                                                                                                                                                                                        |                                                                                         |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                               | <p>24 týdnů – 73,21 %<br/>36 týdnů – 78,71 %</p> <p><u>Průchodnost cév na UZ (průměr %)</u></p> <p>Místo na karotidě</p> <p>12. týdnů 94,6 %<br/>24 týdnů – 96,7 %<br/>36 týdnů – 94,7 %</p> <p>Místa na femorální tepně</p> <p>12 týdnů – 66,9 %<br/>24 týdnů – 63,6 %<br/>36 týdnů – 75,1 %</p> <p>Závěry</p> <ul style="list-style-type: none"> <li>Po 12, 24 nebo 36 týdnech nebyla zjištěna žádná významná známka lokální intolerance (absence viditelných zánětlivých, nekrotických nebo degenerativních lézí).</li> <li>Nebyla zaznamenána žádná významná nežádoucí reakce tkáně mezi hostitelem a prostředkem.</li> <li>Rozklad implantátu byl téměř dokončen za 36 týdnů.</li> </ul> |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002</p> <p>Radi Medical System AB</p> <p>Provedla společnost Biomatech, Francie</p> | <p>Studie na zvířatech</p> | <p>Účelem studie bylo vyhodnotit biokompatibilitu a biologickou funkčnost biologicky rozložitelného implantátu určeného k dosažení hemostázy v cévním systému. Zkoušený prostředek byl určen k zavedení do punkčního otvoru v tepnách za účelem dosažení hemostázy. Jeden disk byl zaveden do punkčního otvoru v tepně a druhý byl připevněn k vnitřnímu disku z vnější strany tepny. Oba disky byly zasunuty přes zaváděcí pouzdro. Disky byly navrženy tak, aby bránily krvácení, vhojily</p> | <p>Doba implantace / následného sledování je u všech zvířat 5 týdnů.</p> <p>4 ovce, 1 prase</p> <p>14 uzavíracích prvků</p> <p>8 uzavíracích prvků implantovaných do 2 ovcí</p> <p>2 uzavírací prvky implantované do 1 prasete</p> <p>Pokud byly dva uzavírací prvky implantovány do stejné femorální tepny, byly implantovány ve vzdálenosti &gt; 30 mm.</p> | <p>Byla zaznamenána kritéria jakýchkoli nežádoucích účinků (zánět, nekróza, krvácení nebo jakákoli jiná léze) nebo vznik jakékoli tenké vrstvy pseudointimy. Zvláštní pozornost byla věnována počáteční tkáňové integraci prostředku se zvláštním důrazem na zapouzdření vnitřního disku.</p> <p>Z makroskopického hlediska nebyly pozorovány žádné významné známky lokální intolerance nebo vzniku trombů. Makroskopické pozorování neodhalilo po implantaci uzavíracích</p>                                                                                                                                                                                                                 |

|  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
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|  |  |  | <p>se do cévní stěny a nakonec se rozložily a byly absorbovány. Studie byla navržena tak, aby po funkční implantaci do ovcí a prasete bylo možné shromáždit a analyzovat data k vyhodnocení schopnosti implantátu zachovat si fyziologickou funkci při použití v oběhovém systému, ke stanovení reakce hostitele a reakce prostředku (fyzikální integrita, zapouzdření tkáně při utracení) a k posouzení rozkladu implantátu.</p> | <p>prvků do femorální tepny žádný rozdíl mezi ovcí a prasetem. Z makroskopického hlediska nebyly pozorovány žádné významné známky lokální intolerance nebo vzniku trombů. Makroskopické pozorování neodhalilo po implantaci uzavíracích prvků do femorální tepny žádný rozdíl mezi ovcí a prasetem.</p> <p>Histopatologická analýza místa implantace u ovcí neprokázala žádné lokální nežádoucí účinky. Vnitřní i vnější disky vykazovaly známky rozkladu a v některých případech byly rozděleny na menší části. Vnitřní disky byly zcela integrovány do neointimální tkáně. U prasete ukázala histopatologická analýza o něco více známek zánětu kolem vnitřních i vnějších disků. U obou zvířat vykazovalo pletené vlákno o něco více známek zánětu než materiál disků, což je u pletených vláken normální z důvodu větší plochy povrchu.</p> <p>Průchodnost cévy byla měřena po 5 týdnech pomocí tří různých metod, histomorfometrie, histomorfometrie v kombinaci s měřením průměru cévy s použitím posuvného měřidla a s použitím barevného dopplerovského ultrazvukového vyšetření. Průměrná průchodnost</p> |
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| <b>První klinická studie u člověka</b>                                                                                                                                                                       |                              |                                                    |                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Název studie                                                                                                                                                                                                 | Rok / hlavní zkoušející      | Typ studie                                         | Cíle                                                                                                                                                                                                                                                                                | Milníky                                                                                                                                                                                                                                                                                                                                               | Potenciální kritéria přijatelnosti                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Otevřené multicentrické hodnocení s jedním ramenem | Cílem studie bylo stanovit bezpečnost, výkon a účinnost systému FemoSeal Vascular Closure System (systému FemoSeal) obecně a konkrétně jeho uzavíracích prvků u pacientů podstupujících diagnostické nebo intervenční kardiologické zákroky využívající přístup do femorální tepny. | Dvoudílná studie<br><br>Celkem n = 80<br>Část 1, n = 20<br>Část 2, n = 60<br><br>Indikace:<br>Část 1 – Diagnostická srdeční katetrizace s použitím femorální tepny jako místa přístupu<br><br>Část 2 – Pacienti podstupující diagnostické a intervenční kardiologické zákroky s použitím femorální tepny jako místa přístupu<br><br>30denní sledování | Výsledky<br><br>– <u>hemostáza dosažena pomocí FS bez komprese</u><br>– Část 1 20/20 (100 %)<br>– Část 2 58/60 (97 %)<br><br>Medián doby do dosažení hemostázy v době zákroku (část 2) – 1,0 minuta (bezprostřední rozsah – 8 minut)<br><br><u>Čas do mobilizace pacienta (minuty)</u><br>Část 1 –<br>medián: 33,0<br>průměr: 67,8<br>Část 2 –<br>medián: 45<br>průměr: 87,5<br><br><u>Výskyt závažných cévních komplikací – 30denní sledování</u><br>Část 1<br>– Bez cévních komplikací 20/20 (100 %)<br>Část 2<br>Pseudoaneuryzma – 1/59 (1,69 %)<br><br><u>Selhání léčby</u><br>Část 1 – 0/20 (0 %)<br>Část 2 – 3/60 (5 %)<br>• 2 z důvodu nedosažení |

|  |  |  |  |  | <p>hemostázy bez použití komprese</p> <ul style="list-style-type: none"> <li>1 z důvodu závažné cévní komplikace, pseudoaneuryzma</li> </ul> <p><u>Trvalé prosakování</u></p> <p>Část 1 – 0/20 (0 %)</p> <p>Část 2 – 8/60 (13 %)</p> <p><u>Hematom</u></p> <p>Část 1 – 0/20 (0 %)</p> <p>Část 2 – 6/60 (10 %)</p> |
|--|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

V rámci plánu klinického vývoje před uvedením systému FemoSeal™ VCS na trh byly provedeny 3 zkoušky funkčnosti na zvířatech. V roce 2000 byla před zahájením klinických studií provedena studie na zvířatech s cílem posoudit biologickou funkčnost systému FemoSeal™ VCS. Tato studie hodnotila schopnost uzavíracích prvků zachovat si fyziologickou funkci a posuzovala jejich rozklad. Po 18 měsících již materiál vnitřního a vnějšího disku nebyl viditelný a byl nahrazen endoluminální fibrózní tkání. V závěru byla schopnost uzavíracího prvku systému FemoSeal™ VCS zachovat si fyziologickou funkci v oběhovém systému potvrzena.

V roce 2002 byla provedena studie na zvířatech za účelem vyhodnocení biokompatibility a biologické funkčnosti biologicky rozložitelného implantátu, systému FemoSeal™ VCS, určeného k zajištění hemostázy v cévním systému. Souhrnně lze říci, že rozklad implantátu byl téměř dokončen do 36 týdnů a nedošlo k žádné významné nežádoucí reakci tkáně.

Biokompatibilitu a biologickou funkčnost biologicky rozložitelného implantátu, systému FemoSeal™ VCS, určeného k zajištění hemostázy v cévním systému, hodnotila v roce 2002 i další studie na zvířatech. Po 5 týdnech bylo zapouzdření disku dokončeno a byly pozorovány známky rozkladu vnitřního i vnějšího disku. V závěru byla schopnost implantátu zachovat si fyziologickou funkci v oběhovém systému potvrzena.

V rámci plánu klinického vývoje systému FemoSeal™ VCS provedla společnost Radi Medical System AB klinickou zkoušku před uvedením na trh. Tato klinická zkouška není zveřejněna ani není k dispozici online. V letech 2002–2004 byla provedena studie s modelem prostředku č. 11200 podle evropské normy EN 540 (Klinické zkoušky zdravotnických prostředků pro humánní účely) a v souladu s Obecnými úvahami ke klinickým hodnocením ICH a pokyny pro správnou klinickou praxi. Podrobnosti o této studii jsou zdokumentovány ve zprávě EU-SE-001. Klinická studie byla zdokumentována v závěrečné zprávě společnosti Radi Medical Systems AB „Multi-

Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures“. Klinická studie byla provedena s prvním modelem prostředku FemoSeal č. 11200 a byla zaměřena na bezpečnost a účinnost implantovatelných uzavíracích součástí. Jediným rozdílem mezi prvním modelem č. 11200 a současným modelem č. C11202 je velikost French, 6F, respektive 7F, a vylepšený systém zavádění. Klinický přínos, určené použití, princip fungování a suroviny implantovatelných uzavíracích prvků, vnitřního uzavíracího a vnějšího zamykacího disku, zůstávají beze změny.

Prostředek byl určen k použití u pacientů podstupujících diagnostické nebo intervenční kardiologické zákroky s využitím femorální tepny jako přístupového bodu. Cílem této studie bylo stanovit bezpečnost, funkčnost a účinnost systému FemoSeal™ VCS. Jednalo se o prospektivní multicentrickou otevřenou studii s jedním ramenem a s 30denním sledováním.

Primárním cílovým ukazatelem funkce byla doba do dosažení hemostázy, která byla definována jako absence aktivního krvácení. Primárním cílovým parametrem bezpečnosti byl výskyt závažných cévních komplikací do 30 dnů. Sekundární cílové parametry zahrnovaly dobu do mobilizace pacienta, míru selhání léčby, výskyt nežádoucích účinků a vlastnosti prostředku z hlediska účinnosti během zavádění a umístění.

Pacienti zařazení do této studie byli dospělí pacienti schopní poskytnout informovaný souhlas, kteří měli alespoň jeden intaktní pulz na arteria dorsalis pedis. Ze studie byli vyloučeni pacienti, kteří měli některý z následujících stavů:

- periferní cévní onemocnění v anamnéze,
- autoimunitní onemocnění,
- známá krvácivá porucha v podobě závažné anemie,
- INR > 1,5,
- infarkt myokardu během 72 hodin,
- nekontrolovaná hypertenze navzdory léčbě,
- obezita bránící přístupu Seldingerovou technikou,
- přítomnost cévního štěpu nebo stentu v místě arteriotomie,
- předchozí ipsilaterální punkce během 3 měsíců,
- očekávaná délka života < 6 měsíců.

Pacienti byli navíc vyšetřováni v průběhu zákroku a pokud byly pozorovány některé z následujících situací, byli ze studie vyřazeni:

- průměr lumen společné femorální tepny < 5 mm,

- arteriální větve ve vzdálenosti do 2 cm proximálně od místa vpichu,
- významná stenóza ve vzdálenosti do 3 cm od místa vpichu,
- použití primárního zaváděcího pouzdra > 6 Fr,
- punkce v místě femorální bifurkace nebo distálně od ní,
- vícenásobná femorální punkce,
- známá nebo suspektní punkce zadní stěny femorální tepny,
- velký hematom (2–6 cm) po dokončení zákroku,
- obtížné zavádění primárního zaváděče k provedení výkonu z důvodu vinuté tkáně nebo cévy.

Tato studie v rámci jednoho protokolu byla provedena ve dvou částech: Během části 1 bylo zařazeno 20 pacientů, poté byla provedena analýza bezpečnosti a během části 2 bylo zařazeno dalších 60 pacientů.

V části 1 byl průměrný věk zařazených pacientů 65,9 let, 70,0 % pacientů byli muži a 95 % pacientů současně užívalo léky. V části 2 studie byl průměrný věk 63,8 let, 78 % byli muži a 100 % pacientů současně užívalo léky.

Pro zařazení do studie byli způsobilí pacienti podstupující zákrok spočívající v diagnostické (část 1 a část 2) nebo intervenční (část 2) srdeční katetrizaci. Zákroky byly v každé z nemocnic účastnících se studie v souladu se standardní péčí a po nich následovalo použití systému FemoSeal™ VCS. Údaje o pacientech byly získány při vstupu do studie, během zákroku a 1 den a 30 dní po zákroku. Výsledky jsou shrnuty v **tabulce 1.5** a ukazují, že systém FemoSeal™ VCS je bezpečný a účinný pro použití u této populace pacientů.

**Tabulka 1.5 Klinické výsledky vykázané ve studii před uvedením na trh**

|                                                  | Část 1      | Část 2                   |
|--------------------------------------------------|-------------|--------------------------|
| Počet pacientů                                   | 20          | 60                       |
| Průměrná doba do dosažení hemostázy              | 1,2 minuty  | 1,6 minuty <sup>a</sup>  |
| Průměrná doba do mobilizace pacienta             | 72,2 minuty | 87,5 minuty <sup>b</sup> |
| Výskyt závažných cévních komplikací <sup>c</sup> | 0 (0 %)     | 1 (2 %)                  |
| Počet pacientů s nežádoucími účinky              | 5 (25 %)    | 19 (32 %)                |

|                                                                                                 |         |          |
|-------------------------------------------------------------------------------------------------|---------|----------|
| Selhání léčby (definované jako závažné cévní komplikace, potřeba manuální komprese, nebo obojí) | 0 (0 %) | 3 (5 %)  |
| Závady prostředku                                                                               | 0 (0 %) | 6 (10 %) |

<sup>a</sup>Na základě vzorku o celkové velikosti 58, protože u 2 pacientů nebylo dosaženo hemostázy v době zákroku z důvodu předchozí ipsilaterální punkce. U těchto pacientů bylo hemostázy dosaženo po 7 minutách a 37 minutách.

<sup>b</sup>Na základě vzorku o celkové velikosti 59: 1 pacient nebyl zařazen, protože byl napojen na ventilátor z důvodu pulmonálního edému a nebyl déle než týden schopen mobilizace.

<sup>c</sup>Definované jako cévní komplikace vyžadující krevní transfuzi nebo chirurgickou opravu nebo lokální infekce vyžadující podání antibiotika, hospitalizaci nebo prodloužení hospitalizace nebo debridement rány.

V části 1 studie nebyly pozorovány žádné významné cévní komplikace. V části 2 studie byla hlášena 1 významná cévní komplikace: pseudoaneuryzma, které bylo hlášeno během jednoho dne po zákroku. Tato příhoda vyžadovala ultrazvukem naváděnou kompresi a injekci trombinu do pseudoaneuryzmatu a prodloužila hospitalizaci pacienta.

Z 5 nežádoucích příhod hlášených v části 1 studie mohla 1 nežádoucí příhoda souviset s prostředkem: nezávažná příhoda aktivního krvácení 1 den po zákroku. Z 19 nežádoucích příhod hlášených v části 2 studie byly pozorovány 3 nezávažné nežádoucí příhody hematomu souvisejícího s prostředkem a 6 nezávažných příhod možná souvisejících s prostředkem, včetně 3 hlášení přetrvávajícího prosakování, 2 hematomů a 1 bolesti nohy po cvičení.

V části 2 byli 3 pacienti považováni za selhání léčby: 2 z důvodu nedosažení hemostázy bez použití komprese a 1 z důvodu závažné cévní komplikace (pseudoaneuryzma). V části 1 studie nedošlo k žádnému selhání léčby.

Ze šesti případů selhání prostředku v části 2 studie tři případy nenarušily zákrok, jeden byl připisován chybě uživatele, jedním byl únik ze zavaděče a jedním zlomený spoj vláken. Poslední dva problémy byly vyřešeny aktualizacemi modelu implementovanými v modelu C11202.

V části 2 klinické studie před uvedením na trh nebyly uvedeny výsledky sledování po 6 měsících v důsledku nespolupráce pacientů. Výsledky klinické studie před uvedením na trh (EU-SE-001) získané v rámci kontroly po 30 dnech, která je v souladu s dobou následného sledování uváděnou v klinické literatuře, ukazují, že systém FemoSeal™ VCS je bezpečný a účinný.

#### 1.4.2 Souhrn údajů z klinických studií po uvedení na trh

V **tabulce 1.6** níže jsou popsány 4 dokončené klinické studie po uvedení na trh. Tato klinická hodnocení nejsou publikována ani nejsou k dispozici online.



**Tabulka 1.6 Realizované klinické studie po uvedení na trh**

| Realizované klinické studie po uvedení na trh                                               |                                                          |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|---------------------------------------------------------------------------------------------|----------------------------------------------------------|-------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|----|-----|----------|-------|----------|-----------|----|----------|-----------|-------------------------|----------|--------------------|------------|---------------------|-----------|-------------------|---------|-----------------------|----------|--------------------------------|----------|----------------------|-----------|--------------------------|-----------|-----------------------------------|----------|----------------------|--------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Název studie                                                                                | Rok / hlavní zkoušející                                  | Typ studie                                                        | Cíle                                                                                                                                                                                                                                                                                                                                                                                                                                              | Milníky                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Potenciální kritéria přijatelnosti                                                                                                          |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI                                             | Studie po uvedení na trh, Přijatelnost nových obalů pro uživatele | Studie provedená s aktualizovaným modelem systému FemoSeal® Vascular Closure System č. 11202, který má upravený systém zavádění ve srovnání s prvním modelem č. 11200, po uvedení na trh za účelem dokumentace funkčnosti.<br><br>Cílem studie bylo získat zpětnou vazbu k revidovanému návodu k použití a ke školicímu projektu pro lékaře a sestry, potvrdit hodnocení provedené v analýze rizik a získat podněty pro zlepšení kvality výrobků. | 100 pacientů <ul style="list-style-type: none"><li>63 mužů / 37 žen</li><li>Průměrný věk u žen 68 let, u mužů 65 let</li></ul> 2 švédské nemocnice, 6 lékařů<br><br>112 prostředků<br><br>Data uvedená ve formulářích se záznamy pacienta (CRF)<br><br>Plánovaná doba pozorování – 30 minut od doby aplikace                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Výsledky<br><br>1. Ilustrace/pokyny v návodu k použití jsou považovány za informativní a odpovídající<br><br>2. Okamžitá hemostáza (91/100) |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)           | Dr. Nicolas Moes, Innsbruck Medical University, Rakousko | Potvrzující hodnocení po uvedení na trh                           | Cílem této studie bylo posoudit bezpečnost a klinickou funkci prostředku FemoSeal® používaného při běžné klinické praxi u pacientů podstupujících diagnostickou srdeční katetrizaci nebo intervenční perkutánní srdeční zákrok prováděný se zaváděčem velikosti 7F.                                                                                                                                                                               | 50 po sobě následujících pacientů<br><br>Indikace – diagnostická nebo invazivní srdeční katetrizace ze společné femorální tepny<br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yr)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                           | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yr) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Primární cílové parametry <ul style="list-style-type: none"><li>Primární cílový parametr účinnosti – doba do dosažení hemostázy s prosakováním nebo bez něj, avšak bez další komprese, manuální nebo mechanické.</li><li>Cílový parametr bezpečnosti – výskyt nežádoucích příhod – drobné a závažné cévní komplikace a všechny další nežádoucí příhody – závažné i nezávažné během trvání studie (tj. až do propuštění pacienta).</li></ul> Výsledky <ul style="list-style-type: none"><li>průměrná doba do dosažení hemostázy,</li><li>Diagnostika – 56,6 ± 29 sekund</li><li>Intervence 59,9 ±16,2 sekundy</li><li>Všichni pacienti 57,8 ± 26,3</li><li>Všechny pacienty bylo možné po 4 hodinách klidu na lůžku bez problémů mobilizovat.</li></ul> |
| n                                                                                           | 50                                                       |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| men                                                                                         | 35 (70%)                                                 |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| women                                                                                       | 15 (30%)                                                 |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| PCI cases                                                                                   | 15                                                       |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| age (yr)                                                                                    | 62.8±11.1                                                |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| body mass index (kg/m²)                                                                     | 25.4±6.7                                                 |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| systolic BP (mmHg)                                                                          | 131.2±20.9                                               |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| diastolic BP (mmHg)                                                                         | 77.9±10.6                                                |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| diabetes mellitus                                                                           | 9 (18%)                                                  |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| arterial hypertension                                                                       | 34 (68%)                                                 |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| previous coronary intervention                                                              | 13 (26%)                                                 |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| preprocedure aspirin                                                                        | 50 (100%)                                                |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| preprocedure clopidogrel                                                                    | 50 (100%)                                                |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Procedural unfractionated heparin                                                           | 15 (30%)                                                 |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Procedural abciximab                                                                        | 2 (4%)                                                   |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |

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|----------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                        |                                        |                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | <p>Výsledky týkající se bezpečnosti</p> <ul style="list-style-type: none"> <li>49/50 (98 %) bez cévních komplikací až do propuštění z nemocnice</li> <li>Průměrná doba do propuštění 2,6 dní</li> <li>1/50 (2 %) menší krvácení druhý den po bezproblémové mobilizaci v den angiografie</li> </ul>                                                                                                                                                                                                                                                                                                              |
| <p>Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)</p>                                                  | <p>2009 RADI</p>                       | <p>Studie po uvedení na trh</p>                                        | <p>Studie měla přinést informace o tom, zda zákazníci/uživatelé pocítují nějaké problémy s novým obalem, zejména s nesterilním vnějším váčkem Tuvek/PET-PE.</p> <p>Studie také měla poskytnout informace o tom, zda ošetřující lékař vnímá nějaké rozdíly v jednotlivých krocích aplikace/zavedení prostředku ve srovnání s dříve použitými prostředky.</p> <p>Studie měla rovněž poskytnout informace o jakýchkoli dalších požadavcích na zvyšování kvality výrobku.</p> | <p>25 prostředků</p> <p>4 švédské nemocnice</p> <p>16/25 (64 %) pacientů byli pacienti PCI se silnými antikoagulačními léky</p>                                                                                                                                                                                                                                                                                                                                      | <p>Výsledky</p> <ol style="list-style-type: none"> <li>Problémy související s obalem – 21/25 (84 %) aplikací bylo úspěšných; 4/25 (16 %) bylo neúspěšných (1 případ testování nového zavaděče, 1 případ průchodu vnitřního disku arteriotomií během zpětného pohybu, tlačítko vyskočilo a vnější disk byl umístěn do kanálu incizní tkáně, 2 případy nedosažení okamžité hemostázy, aniž by nastaly problémy se zavedením).</li> <li>Okamžitá hemostáza 19/25 (76 %) pacientů</li> <li>Krvácení 11/25 (44 %) – prosakování/krvácení 9/25 (36 %), hematomy 2/25 (8 %)</li> </ol> <p>Celková míra příhod 19 %</p> |
| <p>The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022)</p> | <p>2022/Terumo Medical Corporation</p> | <p>Prospektivní multicentrická pozorovací studie po uvedení na trh</p> | <p>Další prokázání bezpečnosti a klinické funkce systému FemoSeal™ VCS při dosahování hemostázy v místech přístupu do společné femorální tepny používaného u reálných pacientů podstupujících perkutánní endovaskulární zákroky</p>                                                                                                                                                                                                                                       | <ul style="list-style-type: none"> <li>Následné sledování pacientů po 30 dnech (<math>\pm</math> 7 dnů) při návštěvě nemocnice nebo telefonickém hovoru.</li> <li>Zařazování: od prosince 2021 do července 2022.</li> <li>230 zařazených subjektů podstupujících diagnostické nebo intervenční endovaskulární zákroky s použitím prostředku FemoSeal™.</li> </ul> <p>3 evropská pracoviště: Francie (92 pacientů), Německo (38 pacientů), Belgie (100 pacientů).</p> | <ul style="list-style-type: none"> <li><b>Demografické údaje / komorbidity:</b></li> <li>- Pohlaví: 161 mužů (70 %)/69 žen (30 %).</li> <li>- Průměrný věk: 70 <math>\pm</math> 12.</li> <li>- BMI: 26,1 <math>\pm</math> 4,95 kg/m<sup>2</sup>.</li> <li>- Hypertenze: 160 pacientů (69,6 %).</li> <li>- Dyslipidemie: 128 (55,7 %).</li> <li>- Ischemická choroba srdeční: 42 (18,3 %).</li> <li>- Současný kuřák: 86 (37,6 %).</li> <li>- Bývalý kuřák: 66 (28,8 %).</li> <li>- Ischemická choroba srdeční: 34 (14 %).</li> </ul>                                                                            |

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|--|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <ul style="list-style-type: none"> <li>- Předchozí infarkt myokardu: 18 (7,8 %).</li> <li>- Revaskularizace periferní tepny: 12 (5,2 %) karotida a 83 (37,5 %) tepna dolní končetiny.</li> <li>- Antiagregační léčba (při vstupu do studie): 211 (91,7 %), včetně 21 (9,1 %) případů duální antiagregační léčby (DAPT).</li> <li>- Perorální antikoagulace: 40 (17,4 %) pacientů.</li> <li>• <b>Charakteristiky zákroku:</b> <ul style="list-style-type: none"> <li>- Prostředí: lůžkové oddělení 162 případů (70,4 %), ambulance 68 případů (29,6 %).</li> <li>- Převažující indikace: klaudikace 147 případů (63,9 %).</li> <li>- Přístup: 35 antegrádní (15,3 %), 194 retrográdní (84,7 %).</li> </ul> </li> <li>• <b>Primární cílové parametry:</b> <ul style="list-style-type: none"> <li>- Kombinovaného cílového parametru bezpečnosti (nepřítomnost závažných komplikací v místě přístupu do 6 hodin po zákroku) a účinnosti (úspěšná hemostáza v místě vpichu) bylo dosaženo u 215/226 (95,1 %) [95% CI: 91,46; 97,55] pacientů v plně analyzovaném souboru a u 215/230 (93,5 %) [95% CI 89,47; 96,30] pacientů v souboru léčeném prostředkem FemoSeal™.</li> <li>- Cílového parametru účinnosti bylo dosaženo u 219/226 (96,9 %) CI [93,7; 98,7] pacientů.</li> <li>- Cílového parametru bezpečnosti bylo dosaženo u 220/230</li> </ul> </li> </ul> |
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|--|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <p>(95,2 %) [95% CI: 92,15; 97,90] pacientů.</p> <ul style="list-style-type: none"> <li>• <b>Sekundární cílové parametry:</b> <ul style="list-style-type: none"> <li>- Nepřítomnosti menších komplikací v místě přístupu po dobu šesti hodin od zákroku bylo dosaženo u 225/230 (97,8 %) [95% CI: 95,00; 99,29] pacientů.</li> <li>- Nepřítomnosti závažných a menších komplikací v místě přístupu po dobu šesti hodin až 30 dní od zákroku bylo dosaženo u 219/230 (95,2 %) [95% CI: 91,60; 97,59] pacientů.</li> <li>- Medián doby do dosažení hemostázy s prostředkem FemoSeal™ VCD: 0,42 (0,25; 0,50) minut.</li> <li>- Medián doby do mobilizace pacienta: 5,00 (4,54; 5,50) minut.</li> <li>- Medián doby pobytu v nemocnici: 23,98 (22,72; 25,00) hodin.</li> <li>- Použitelnost systému FemoSeal™ VCS: „snadné“ nebo „velmi snadné“ zavedení v 98,7 % případů („snadné“ zavedení v 21 případech (9,2 %), „velmi snadné“ zavedení ve 205 případech (89,5 %)) s nulovým nebo nízkým odporem při zavádění ve 226 případech (98,3 %).</li> </ul> </li> </ul> <p>152/230 (66,1 %) pacientů léčeno pomocí vodicího drátu, který je součástí soupravy FemoSeal™ (GW 0,038") a doporučený v soupravě FemoSeal™, bez jakýchkoli hlášených nedostatků prostředku nebo nežádoucích příhod.</p> |
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Studie z roku 2006 byla provedena za účelem potvrzení bezpečnosti a účinnosti současného prostředku s vylepšeným zaváděcím systémem a získání zpětné vazby k návodu k použití a školicímu programu systému FemoSeal™ VCS. Studie zahrnovala 100 pacientů a primárním cílovým ukazatelem bylo, zda bylo dosaženo hemostázy, nebo zda byla nutná další manuální nebo mechanická komprese. Tato studie dospěla k závěru, že použití systému FemoSeal™ VCS bylo ve většině případů úspěšné (v 91 % případů bylo dosaženo okamžité hemostázy).

Do studie z roku 2008 bylo zařazeno 50 pacientů za účelem posouzení bezpečnosti a klinické funkce systému FemoSeal™ VCS při použití v běžné klinické praxi u pacientů podstupujících srdeční katetrizaci se zaváděčem 7F. Primárním cílovým ukazatelem studie bylo shromáždit údaje o době do dosažení hemostázy a době do mobilizace pacienta bez další komprese, manuální nebo mechanické. Z výsledků studie vyplynul závěr, že průměrná doba do dosažení hemostázy činila 57,8 sekund a všichni pacienti byli mobilizováni po 4 hodinách klidu na lůžku.

Studie z roku 2009 byla zaměřena na hodnocení nového obalu systému FemoSeal™ VCS. Do studie bylo zařazeno 25 pacientů. Primárním cílovým parametrem bylo, zda uživatel zaznamenal jakékoli problémy s obalem. Uživatelé nezaznamenali žádné problémy týkající se nového obalu systému FemoSeal™ VCS. Tato studie také shromažďovala údaje o době do dosažení hemostázy.

Cílem studie z roku 2022 bylo aktivně shromáždit údaje o bezpečnosti a účinnosti systému FemoSeal VCS při dosahování hemostázy v místech přístupu do společné femorální tepny používaného při běžné klinické praxi u reálných pacientů podstupujících perkutánní endovaskulární zákroky. Do studie bylo zařazeno 230 pacientů. Primárními cílovými parametry registru jsou úspěch zákroku (tj. úspěšná hemostáza v místě vpichu) a snížení počtu závažných komplikací (např. cévní poranění, krvácení související s místem přístupu, infekce v místě přístupu, opakovaná manuální komprese a nová akutní ipsilaterální ischemie dolních končetin v místě přístupu). Studie dospěla k závěru, že systém FemoSeal™ VCS funguje v reálném prostředí dobře a u pacientů podstupujících periferní endovaskulární zákroky poskytuje účinnou hemostázu a nízkou míru komplikací v místě přístupu. Vykazuje dobrou funkčnost s krátkou dobou do dosažení hemostázy a dobrou zpětnou vazbu operátora, díky čemuž je systém FemoSeal™ VCS cenným prostředkem pro uzavírání femorálního přístupu.

### **1.4.3 Souhrn údajů z klinických studií po uvedení na trh**

#### **1.4.3.1 Dokončené klinické sledování po uvedení na trh**

Souhrn dokončených činností klinického sledování po uvedení na trh je popsán v **tabulce 1.7** níže.

**Tabulka 1.7. Následné klinické činnosti po uvedení na trh**

| Realizované následné klinické činnosti po uvedení na trh                  |                         |                                                              |                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|---------------------------------------------------------------------------|-------------------------|--------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <u>Název činnosti</u>                                                     | Rok / hlavní zkoušející | Typ studie                                                   | Cíle                                                                                                                                                                                                                                                             | Milníky                                                                                                                                                                                                                                                                                                                  | Potenciální kritéria přijatelnosti                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021 TMC                | Klinický průzkum po uvedení na trh – vysoce kvalitní průzkum | Průzkum po uvedení na trh za účelem shromáždění prospektivní zpětné vazby týkající se použití prostředku FemoSeal™ Vascular Closure Device distribuovaného na trzích Evropské unie.                                                                              | <ul style="list-style-type: none"> <li>120 případů</li> <li>8 vynikajících lékařů s &gt; 5letou praxí</li> <li>Několik zemí v Evropě</li> </ul>                                                                                                                                                                          | <b>Hodnocení prostředku na škále 1–5 – Výsledky průzkumu</b> <ul style="list-style-type: none"> <li>Kritéria pro přijetí <ul style="list-style-type: none"> <li>Hodnocení 3–5 jsou považována za příznivá</li> <li>Všechny výsledky by měly mít <math>\geq 80\%</math> pozitivní zpětnou vazbu</li> </ul> </li> <li>Výsledky <ul style="list-style-type: none"> <li>Nebyl obdržěn žádný výsledek průzkumu, který by měl &gt; 20 % nepříznivých reakcí</li> <li>Nebyly podány žádné reklamace týkající se výrobku</li> </ul> </li> </ul> |
| 20210298 – 0,035" and 0038" Guidewire Clinical Survey Report (2021)       | 2021 TMC                | Klinický průzkum po uvedení na trh – vysoce kvalitní průzkum | Průzkum po uvedení na trh za účelem shromáždění prospektivní zpětné vazby týkající se použití vodícího drátu 0,035" obsaženého v prostředku 6Fr Angio-Seal™ VIP Vascular Closure Device (VCD) a 0,038" obsaženého v prostředku 8Fr Angio-Seal™ VIP VCD a systému | <ul style="list-style-type: none"> <li>Průzkumy pro 0,035" drát <ul style="list-style-type: none"> <li>106 průzkumů</li> <li>64 lékařů</li> </ul> </li> <li>Průzkumy pro 0,038" drát <ul style="list-style-type: none"> <li>109 průzkumů</li> <li>55 lékařů</li> </ul> </li> <li>12 retrospektivních průzkumů</li> </ul> | <b>Hodnocení prostředku na škále 1–5 – Výsledky průzkumu</b> <ul style="list-style-type: none"> <li>Kritéria pro přijetí <ul style="list-style-type: none"> <li>Hodnocení 3–5 jsou považována za příznivá</li> <li>Všechny výsledky by měly mít <math>\geq 80\%</math> pozitivní zpětnou vazbu</li> </ul> </li> <li>Výsledky <ul style="list-style-type: none"> <li>Všechny vodící dráty obdržely přijatelná hodnocení</li> <li>Nebyly podány žádné reklamace</li> </ul> </li> </ul>                                                    |

| Realizované následné klinické činnosti po uvedení na trh                                                                        |                     |                                                              |                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                     | týkající se výrobku                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|---------------------------------------------------------------------------------------------------------------------------------|---------------------|--------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024<br>TMC/TE | Klinický průzkum po uvedení na trh – vysoce kvalitní průzkum | FemoSeal Vascular Closure System distribuovaných na trzích Evropské unie.<br><br>Prospektivní shromažďování zpětné vazby týkající se použití systému FemoSeal VCS s vodícími dráty distribuovanými na trhu EU. | <ul style="list-style-type: none"> <li>126 průzkumů</li> <li>7 pracovišť</li> <li>5 zemí</li> <li>14. listopadu 2023 – 11. června 2024</li> <li>Odbornost lékaře: <ul style="list-style-type: none"> <li>Cévní chirurgie</li> <li>Intervenční radiologie</li> <li>Angiologie</li> </ul> </li> </ul> | <b>Hodnocení prostředku na škále 5 – Výsledky průzkumu</b> <ul style="list-style-type: none"> <li>Kritéria pro přijetí <ul style="list-style-type: none"> <li>Hodnocení 3–5 jsou považována za příznivá</li> <li>Všechny výsledky by měly mít <math>\geq 80\%</math> pozitivní zpětnou vazbu</li> <li>Pokud se v tomto průzkumu vyskytnou nežádoucí příhody, měly by být těmi, které předpokládá řízení rizik.</li> </ul> </li> <li>Demografické údaje pacientů <ul style="list-style-type: none"> <li>Ženy: 29,4 % (37/126)</li> <li>Muži: 69,8 % (88/126)</li> <li>Pohlaví není uvedeno: 0,8 (1/126)</li> <li>Věk &gt; 75 let: 31,7 %</li> </ul> </li> <li>Výsledky <ul style="list-style-type: none"> <li>Vodící drát dodávaný s FemoSeal™ VCS: 101/126 (80,2 %).</li> <li>Doba procedury (v minutách): 63,4 (36,6) (průměr (SD));</li> </ul> </li> </ul> |

| Realizované následné klinické činnosti po uvedení na trh |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|----------------------------------------------------------|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                          |  |  |  |  | 57,0 (36,0-81,0)<br>(medián (IQR)) <ul style="list-style-type: none"> <li>○ Všechna hodnocení výkonu systému FemoSeal™ VCS byla příznivá.</li> <li>○ Všechna hodnocení vodícího drátu dodávaného se systémem FemoSeal™ VCS byla příznivá.</li> <li>○ Jedna nežádoucí příhoda (0,8 %): disky systému FemoSeal™ VCS nebyly správně vyrovnány pravděpodobně kvůli použití tuhého vodícího drátu (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 palce), který vyžadoval manuální kompresi k dosažení hemostázy.</li> </ul> |

Společnost Terumo Medical Corporation provedla tři vysoce kvalitní průzkumy mezi lékaři a uživateli během aktuálního vykazovaného období (od 01. září 2019 do 31. srpna 2024).

V klinických průzkumech týkajících se prostředku FemoSeal™ byly shromážděny proaktivní klinické údaje ohledně bezpečnosti a klinické funkce systému FemoSeal™ VCS při klinickém použití. Průzkum zahrnoval otázky zaměřené na prostředek jako celek i na jeho související příslušenství včetně vodícího drátu o průměru 0,038" a jejich přímé interakce. V klinických průzkumech týkajících se vodícího drátu byly shromážděny proaktivní klinické údaje ohledně



bezpečnosti a klinické funkce při klinickém použití vodicího drátu o průměru 0,038" dodávaného se systémem FemoSeal™ VCS. Otázky průzkumu byly konkrétně zaměřeny na obecné použití vodicího drátu od jeho zavedení přes zavaděč do cévního systému až po odstranění drátu.

Systém FemoSeal™ VCS a vodicí drát o průměru 0,038", který je součástí prostředku, získal všechna přijatelná hodnocení. Na základě vyhodnocení komentářů získaných ve vysoce kvalitních klinických průzkumech bylo podáno šest (6) stížností týkajících se prostředku a devět (9) jiných komentářů týkajících se vodicího drátu. Stížnosti jak na prostředek FemoSeal, tak na vodicí drát byly vyhodnoceny a byly posouzeny v rámci procesu sledování společnosti Terumo po uvedení na trh. Nebyla identifikována žádná nová rizika nebo úrovně rizika.

V roce 2024 byl v rámci činností PMCF proveden průzkum mezi lékaři a uživateli. Výsledky průzkumu prokázaly, že hodnocení výkonu a bezpečnosti systému FemoSeal™ VCS je celkově velmi příznivé. Byla také prokázána kompatibilita s jinými vodicími dráty než s těmi, které jsou standardně dodávány s prostředkem FemoSeal™ VCS.

#### **1.4.3.2 Probíhající/plánovaná následná klinická sledování po uvedení na trh**

Společnost TMC provádí jednu probíhající/plánovanou klinickou činnost v rámci následného sledování po uvedení na trh. Bude proveden klinický průzkum, který bude výhledově zaměřen na získání zpětné vazby týkající se používání vodicího drátu se systémem FemoSeal VCS distribuovaným na trhu EU. Průzkum budou vyplňovat lékaři, kteří uvedou, jaké vodicí dráty během výkonu používali. Účelem tohoto průzkumu je vyřešit mezeru identifikovanou jako nedostatek literatury a komentářů externích recenzentů ke kompatibilitě systému FemoSeal™ VCS s použitím vodicích drátů jiných značek než Terumo. Zpětná vazba bude zahrnovat technické výsledky, klinickou funkci a bezpečnost související s funkčností prostředku s různými vodicími dráty.

#### **1.4.4 Souhrn údajů ze systematického přezkoumání literatury**

Společnost Terumo Medical Corporation provádí systematický přezkum literatury za účelem shromažďování a vyhodnocování údajů o klinické bezpečnosti a funkci z publikovaných studií týkajících se prostředku FemoSeal™ VCS a/nebo podobných prostředků. Cílem každoročního screeningu publikované literatury je identifikace dříve neznámých vedlejších účinků, sledování známých nežádoucích účinků, identifikace vzniklých rizik a identifikace možného systematického nesprávného použití nebo použití prostředku FemoSeal™ VCS mimo rozsah rozhodnutí o registraci.

Nejnovější systematický přezkum literatury, který zahrnoval období od 1. září 2019 do 31. srpna 2024, identifikoval 29 publikovaných studií, které poskytly údaje o klinické bezpečnosti a funkci prostředku FemoSeal™ VCS. V devíti studiích bylo hlášeno dvacet tři referencí použití systému FemoSeal™ VCS v rozsahu a mimo rozsah rozhodnutí o registraci. Celkově lze říci, že přehled literatury u studií specifických pro použití systému FemoSeal™ VCS ukazuje ve studiích

populaci, která je reprezentativní pro pacienty v EU podstupující perkutánní katetrizační zákroky. Seznam těchto 23 recenzovaných publikací v rozsahu rozhodnutí o registraci naleznete v **části 3.**

Klinická funkce byla posouzena na základě následujících parametrů:

- Doba do dosažení hemostázy je lepší nebo srovnatelná s nejnovějšími technologiemi uzavření společné femorální tepny po perkutánním zákroku.
- Doba do mobilizace je lepší nebo srovnatelná s nejnovějšími technologiemi uzavření společné femorální tepny po perkutánním zákroku.
- Míra pooperačních komplikací je srovnatelná nebo nižší než při současné standardní péči.

Na základě těchto ukazatelů klinické funkce vyplynulo z údajů v tomto přehledu literatury, že systém FemoSeal™ VCS lze úspěšně používat k uzavření femorální arteriální punkce (arteriotomie) u pacientů, kteří podstoupili perkutánní katetrizaci s použitím zavaděče velikosti 7F nebo menšího. Úplné hemostázy bylo dosaženo u většiny pacientů (79,65-100 %) a byla spojena s mediánovou dobou do dosažení hemostázy 0,5 minuty a průměrnou dobou do propuštění z nemocnice 3 dny. Od 69,2 do 86,7 % pacientů bylo schopno pohybovat se 5 hodin po uzavření, přičemž průměrná doba pooperačního odpočinku na lůžku byla 349 minut. Selhání systému FemoSeal™ VCS bylo pozorováno v 3,68-4 % případů a dodatečná manuální komprese byla potřebná v 0,9-4,4 % případů.

Klinická bezpečnost byla posouzena na základě nežádoucích příhod, které zahrnovaly mimo jiné:

- Krvácení
- Hematom
- Pseudoaneuryzma
- Odřenniny
- Arteriovenózní píštěl
- Infekce
- Smrt

U každého z těchto nežádoucích účinků byla míra výskytu hlášena při použití systému FemoSeal™ VCS v rámci zahrnutých studií nižší nebo srovnatelná s historicky hlášenými mírami při použití manuální komprese a jiných prostředků na uzavírání cév.

Při přezkumu 10 kazuistik nebyly zjištěny žádné nežádoucí účinky, neboť nebyla identifikována žádná nová, neočekávaná, vznikající nebo nepříjemná rizika.

Celková účinnost použití systému FemoSeal™ VCS během diagnostické angiografie nebo intervenčních operací závisí na několika faktorech, jako je pohlaví, věk, anatomie pacienta, komorbidita, anatomické umístění místa vpichu, zkušenosti chirurga, metoda zavedení VCD,

pooperační péče, atd. Kromě technického úspěchu, včetně dosažení hemostázy, nabízel systém FemoSeal™ VCS klinický přínos ve vztahu k uzavření cévy po vpichu do femorální tepny, jako je zkrácení doby do dosažení hemostázy a zkrácení doby do chůze. Výsledky týkající se klinické funkce prostředku FemoSeal™ VCS jsou v souladu s výsledky očekávanými u tohoto typu prostředku při použití v souladu s určeným účelem. Některé reference získané během aktuálního období vyhledávání ukázaly použití předmětného prostředku v jiném anatomickém umístění než ve společné femorální tepně a pro uzavření arteriotomií > 7 Fr, což je považováno za použití mimo rozsah rozhodnutí o registraci.

Během revize nebyly zjištěny žádné neznámé vedlejší účinky, nově vznikající rizika nebo možné systematické nesprávné použití prostředku. Nicméně pokud je systém FemoSeal™ VCS používán s opatrností vyškolenými lékaři, funguje zdravotnický prostředek jako užitečný a nezbytný klinický prostředek. Celkově cílová terapie, a tudíž systém FemoSeal™ VCS, řeší klinickou potřebu, která v současné době existuje při léčbě komplikací souvisejících s cévním přístupem.

Celkově lze říci, že v údajích v tomto přehledu literatury nebyly zjištěny žádné problémy s klinickou funkcí nebo bezpečností v klinickém prostředí, které by dříve byly neznámé, ani nežádoucí účinky, ke kterým by došlo ve vyšší míře, než se předpokládá / než je přijatelné. Z tohoto přehledu literatury lze proto vyvodit závěr, že systém FemoSeal™ VCS při použití k zajištění komprese pro dosažení hemostázy při arteriotomii po perkutánní katetrizaci funguje i nadále dle očekávání a není spojen s vážnými bezpečnostními příhodami.

#### 1.4.5 Souhrn údajů ze sledování po uvedení na trh

Je zaveden systém aktivního sledování po uvedení na trh a každý měsíc se provádí přezkum všech reklamací v souladu s interními výrobními postupy. Údaje o reklamacích byly analyzovány v období od 1. září 2019 do 31. srpna 2024. Celkově bylo výrobcí předloženo 28 hlášení v rámci vigilance pro zdravotnické prostředky (MDV) a 476 hlášení o zákaznických reklamacích. Z 28 hlášení MDV souviselo 27 s nežádoucími účinky a jeden s poruchou prostředku. Během vykazovaného období došlo ke dvěma úmrtím, ale žádné z hlášených úmrtí nebylo považováno za související s předmětným prostředkem. Ze 476 reklamací podaných výrobcí byly nejčastějšími důvody obtíže při nasazení (146 výskytů, četnost výskytu 0,0142 %). Druhým nejčastějším výskytem je poruchový režim příhod vytažení s četností 0,0126 % (130 událostí).

V celém světě bylo prodáno více než 1 030 136 prostředků FemoSeal™ Vascular Closure System, z toho 827 843 v Evropském hospodářském prostoru. Vypočítaná četnost reklamací na základě celosvětového prodeje je 0,046 %. Celková míra reklamací zákazníků je velmi nízká. Nebyla zjištěna žádná nová rizika, která by nebyla uvedena v návodu k použití a v dokumentaci týkající se rizik.

Frekvence výskytu nežádoucích účinků je uvedena v **tabulce 1.2**. Nebyla identifikována žádná nová nepředvídaná, vznikající nebo nepřijatelná rizika. Nebylo pozorováno žádné významné zvýšení četnosti nebo závažnosti známých nežádoucích vedlejších účinků.

#### 1.4.6 Celkový souhrn údajů o klinické funkci a bezpečnosti

Systém FemoSeal™ VCS je indikován k použití při uzavírání punkce společné femorální tepny (arteriotomie) u pacientů, kteří podstoupili perkutánní katetrizaci pomocí zavaděče velikosti 7F (2,33 mm) nebo menšího. Toto klinické hodnocení vychází z komplexní analýzy dostupných klinických údajů před uvedením na trh a po uvedení na trh a z literatury týkající se určeného použití prostředku FemoSeal™ VCS.

Byl proveden komplexní přezkum literatury publikované v období od 1. září 2019 do 31. srpna 2024. Soubor důkazů zahrnoval 29 studií týkajících se prostředku FemoSeal™ VCS. Z důkazů poskytnutých v klinickém hodnocení lze učinit závěr, že dotčený prostředek je při použití v souladu s určeným použitím bezpečný a účinný a veškerá rizika nebo nežádoucí účinky, které mohou být za normálních podmínek použití s prostředkem spojeny, představují při zvážení přínosů pro pacienta přijatelná rizika. Výsledky týkající se klinické funkce dotčených prostředků jsou v souladu s výsledky očekávanými u tohoto typu prostředku při použití v souladu s určeným účelem.

Potenciální nežádoucí účinky spojené s použitím systému FemoSeal™ VCS zahrnují nežádoucí příhody běžně hlášené u alternativních prostředků na uzavření arteriotomie, např. krvácení a hematom. Celkově byla frekvence výskytu nežádoucích příhod hlášených při použití systému FemoSeal™ VCS podobná jako frekvence hlášené při použití manuální komprese a podobných prostředků na uzavírání cév. Konkrétně u krvácení a hematomu byla frekvence hlášená při použití systému FemoSeal™ VCS nižší než frekvence hlášené při použití podobných prostředků na uzavírání cév. Všechny nahlášené nežádoucí příhody, jak z publikované literatury, tak i ze sledování po uvedení na trh, byly identifikovány již dříve (viz **část 1.3**).

Stávající údaje týkající se klinické bezpečnosti a funkce systému FemoSeal™ VCS naznačují, že přínosy použití tohoto prostředku na uzavírání cév pro pacienta převažují nad jeho možnými riziky, pokud je používán v souladu s návodem k použití.

Jak je uvedeno v předchozích částech výše, údaje získané o prostředku FemoSeal™ VCS prokazují soulad mezi údaji týkajícími se hodnoceného prostředku (např. použití prostředku, výsledky týkající se bezpečnosti, klinická funkce a klinické přínosy), identifikovanými ekvivalentními prostředky a údaji souvisejícími s podobnými prostředky dle nejnovějšího vývoje.

Křížová analýza údajů o bezpečnosti neodhalila žádné nesrovnalosti mezi následujícími:

- Údaji uvedenými v analýze nejnovějšího vývoje
- Údaji specifickými pro hodnocený prostředek
- Údaji uvedenými v souboru/souborech řízení rizik

- Údaji uvedenými v označení a/nebo v návodu k použití (tj. jsou uvedena zbytková rizika, která mají být sdělena uživateli).

Klinická bezpečnost byla prokázána nízkými četnostmi komplikací zjištěnými v publikované recenzované klinické literatuře, v klinických studiích zadaných společnostmi, při přezkumu údajů po uvedení na trh a skutečností, že nedošlo k žádnému stažení z trhu. Nebyly zjištěny žádné obavy v souvislosti s klinickou funkcí, literatura hodnotila dlouhodobé použití prostředku FemoSeal™ VCS, které bylo v souladu s použitím určeným výrobcem.

### 1.5 Možné diagnostické nebo léčebné alternativy

K dosažení hemostázy v místě arteriotomie po cévní katetrizaci se tradičně používá manuální komprese. Manuální komprese je spojena s delší imobilizací pacienta (až 8 hodin po zákroku) a se značným nepohodlím a delším pobytem v nemocnici. V jednom nedávném systematickém přezkumu bylo zjištěno, že medián doby pro dosažení hemostázy s manuální kompresí je 20,8 minuty.<sup>1</sup>

K alternativám manuální komprese patří externí hemostatické prostředky, které v místě arteriotomie aplikují mechanickou kompresi. Tyto prostředky nezkracují dobu do dosažení hemostázy ani dobu do mobilizace pacienta, ale snižují nároky na personál nahrazením manuální komprese mechanickou kompresí. Míra nežádoucích příhod spojených s použitím mechanické komprese je podobná jako u manuální komprese.

Prostředky na uzavírání cév, jako je systém FemoSeal™ VCS, jsou určeny k uzavírání arteriotomie. Jejich účelem je zkrácení doby do dosažení hemostázy a umožnění dřívější mobilizace pacienta. V jednom nedávném systematickém přezkumu zaměřeném na 13 komerčně dostupných prostředků bylo zjištěno, že medián doby do dosažení hemostázy s prostředkem na uzavírání cév je 5,4 minut. Medián doby do dosažení hemostázy se u jednotlivých prostředků na uzavírání cév pohyboval v rozmezí od 1 minuty (systém FemoSeal™ VCS) do 14 minut, přičemž většina prostředků se pohybovala mezi 4 a 10 minutami.<sup>1</sup>

Mezi běžně hlášené nežádoucí příhody spojené s uzavřením místa arteriotomie, s manuální kompresí, externími hemostatickými prostředky nebo prostředky na uzavírání cév patří hematoma, krvácení v místě přístupu, pseudoaneuryzma, arteriovenózní píštěl a infekce. Ve stejném systematickém přezkumu (34 randomizovaných kontrolovaných studií, 14 401 pacientů) bylo zjištěno, že míra nežádoucích účinků byla u manuální komprese a při použití prostředků na uzavírání cév podobná, s výjimkou toho, že krvácení bylo při použití prostředků na uzavírání cév o něco vyšší.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Doporučený profil uživatele a školení uživatele

Určenými uživateli systému FemoSeal™ Vascular Closure System jsou lékaři, kteří jsou vyškoleni v oblasti vytváření a uzavírání arteriálního přístupu k provádění endovaskulárních výkonů přes společnou femorální tepnu a absolvovali školicí program pro lékaře o prostředku FemoSeal™ společnosti Terumo Medical Corporation.

## 1.7 Relevantní harmonizované a společné normy

| Označení normy | Aktuální rok shody/revize | Popis                                                                                                                                    |
|----------------|---------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070      | 2014/AMD1:2018            | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070   | 2014/A1:2018              | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance   | 20. května 2021           | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052     | 2015                      | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213     | 2017                      | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503     | 2020                      | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182     | 2019                      | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |
| EN ISO 13485   | 2016/A11:2021             | Medical devices – Quality management systems – Requirements for regulatory purposes                                                      |
| ISO 13485      | 2016                      | Medical devices – Quality management systems – Requirements for regulatory purposes                                                      |



| Označení normy | Aktuální rok shody/revize | Popis                                                                                                                                                                    |
|----------------|---------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14644-1    | 2015                      | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1 | 2015                      | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2    | 2015                      | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2 | 2015                      | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3    | 2019                      | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3 | 2019                      | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1    | 2003                      | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1 | 2003                      | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2    | 2003/TC1:2004             | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| EN ISO 14698-2 | 2003/TC 1:2004            | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| USP <788>      | Nerelevantní              | PARTICULATE MATTER IN INJECTIONS                                                                                                                                         |

| Označení normy    | Aktuální rok shody/revize | Popis                                                                                                                |
|-------------------|---------------------------|----------------------------------------------------------------------------------------------------------------------|
| Lékopis EU 2.9.19 | Nerelevantní              | Particulate Contamination: Sub-Visible Particles                                                                     |
| IEC 62366-1       | 2015                      | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN 62366-1        | 2015                      | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN ISO 14971      | 2019/A11:2021             | Medical devices — Application of risk management to Medical devices                                                  |
| ISO 14971         | 2019                      | Medical devices — Application of risk management to Medical devices                                                  |
| ASTM F1980        | 2016                      | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1    | 2020                      | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1       | 2018                      | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2    | 2006                      | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2       | 2006                      | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3    | 2014                      | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3       | 2014                      | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4    | 2017                      | Biological Evaluation of Medical Devices – Part 4: Selection of tests for interactions with blood                    |
| ISO 10993-4       | 2017                      | Biological Evaluation of Medical Devices – Part 4: Selection of tests for interactions with blood                    |



| Označení normy  | Aktuální rok shody/revize | Popis                                                                                                                                      |
|-----------------|---------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-5  | 2009                      | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                                         |
| ISO 10993-5     | 2009                      | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                                         |
| EN ISO 10993-6  | 2016                      | Biological evaluation of medical devices – Part 6: Tests for local effects after implantation                                              |
| ISO 10993-6     | 2016                      | Biological evaluation of medical devices – Part 6: Tests for local effects after implantation                                              |
| EN ISO 10993-10 | 2023                      | Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization                                            |
| ISO 10993-10    | 2021                      | Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization                                            |
| EN ISO 10993-11 | 2018                      | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| ISO 10993-11    | 2017                      | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| EN ISO 10993-12 | 2021                      | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| ISO 10993-12    | 2021                      | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| EN ISO 10993-17 | 2009                      | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17    | 2002                      | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18    | 2020/A1:2022              | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |

| Označení normy  | Aktuální rok shody/revize | Popis                                                                                                                                                                        |
|-----------------|---------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-18 | 2020/A1:2022              | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-23 | 2021                      | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23    | 2021                      | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382      | 2018                      | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756       | 2017                      | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>        | Nerelevantní              | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>       | Nerelevantní              | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72  | 2019                      | Bacterial endotoxins – Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135    | 2014/A1:2019              | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135       | 2014/A1:2018              | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7  | 2008/A1:2022              | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |

| Označení normy | Aktuální rok shody/revize | Popis                                                                                                                                                           |
|----------------|---------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-7    | 2008/A1:2019              | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                               |
| EN 556-1       | 2024                      | Sterilization of medical devices – Requirements for medical devices to be designated "STERILE" – Part 1: Requirements for terminally sterilized medical devices |
| EN ISO 11737-1 | 2018/A1:2021              | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11737-1    | 2018/A1:2021              | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| EN ISO 11138-1 | 2017                      | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-1    | 2017                      | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| EN ISO 11138-2 | 2017                      | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 11138-2    | 2017                      | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| EN ISO 15223-1 | 2016                      | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| ISO 15223-1    | 2016                      | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| EN 1041        | 2008/A1:2013              | Information supplied by the manufacturer of medical devices                                                                                                     |
| EN ISO 11607-1 | 2020/A1:2023              | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                         |

| Označení normy    | Aktuální rok shody/revize | Popis                                                                                                                                                                      |
|-------------------|---------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11607-1       | 2019/A1:2023              | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| EN ISO 11607-2    | 2020/A1:2023              | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ISO 11607-2       | 2019/A1:2023              | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169        | 2016                      | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M | 2016                      | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825        | 2018                      | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096        | 2011 (R 2019)             | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M     | 2015                      | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24      | 2021                      | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3       | 2020                      | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |
| MDCG 2020-8       | 2020                      | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                             |
| MDCG 2020-7       | 2020                      | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                          |

| Označení normy | Aktuální rok shody/revize | Popis                                                                                                                                                                                                                                                         |
|----------------|---------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-6    | 2020                      | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                                                                                                          |
| MDCG 2019-9 v1 | 2022                      | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                                                                                      |
| MDCG 2019-8 v2 | 2020                      | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15   | 2020                      | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11   | 2021                      | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19   | 2021                      | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4 | 2021                      | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2    | 2019                      | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1    | 2019                      | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7    | 2018                      | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6    | 2018                      | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |

| Označení normy         | Aktuální rok shody/revize | Popis                                                                                                                                                                                         |
|------------------------|---------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2018-4            | 2018                      | MDCG 2018-4 Annex: UDI database<br>Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                               |
| MDCG 2018-3<br>v1      | 2020                      | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25           | 2021                      | Regulation (EU) 2017/745 – application of MDR requirements to ‘legacy devices’ and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2.12-2<br>Rev 2 | 2012                      | Guidance document Medical devices – Market surveillance – Post Market Clinical Follow-up studies – MEDDEV 2.12/2 rev.2                                                                        |

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### 3.0 HISTORIE REVIZÍ

| Číslo revize SSCP       | Datum vydání    | Popis změny                                                     | Revize ověřená oznámeným subjektem                                                                                                                                                                                                                                                                                                                   |
|-------------------------|-----------------|-----------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022            | 20. ledna 2023  | První vydání, na základě osvědčení CE podle MDR                 | <p><input checked="" type="checkbox"/> Ano</p> <p>Jazyk ověření: English</p> <p><input type="checkbox"/> Ne (platí pouze u prostředků třídy IIa nebo některých implantovatelných prostředků třídy IIb (MDR, článek 52 (4) 2. odstavec), u kterých dosud není ověřeno SSCP oznámeným subjektem)</p> <p><input type="checkbox"/> Jiné (upřesněte):</p> |
| SSCP-FS-2023 – Revize 1 | 15. března 2024 | Aktualizováno pro období od 1. ledna 2019 do 31. prosince 2023. | <p><input checked="" type="checkbox"/> Ano</p> <p>Jazyk ověření: English</p> <p><input type="checkbox"/> Ne (platí pouze u prostředků třídy IIa nebo některých implantovatelných prostředků třídy IIb (MDR, článek 52 (4) 2. odstavec), u kterých dosud není ověřeno SSCP oznámeným subjektem)</p> <p><input type="checkbox"/> Jiné (upřesněte):</p> |
| SSCP-FS-2024 Revize 1   |                 | Aktualizováno pro období od 1. září 2019 do 31. srpna 2024.     | <p><input type="checkbox"/> Ano</p> <p>Jazyk ověření: English</p> <p><input type="checkbox"/> Ne (platí pouze u prostředků třídy IIa nebo některých implantovatelných prostředků třídy IIb (MDR, článek 52 (4) 2. odstavec), u kterých dosud není ověřeno SSCP oznámeným subjektem)</p> <p><input type="checkbox"/> Jiné (upřesněte):</p>            |

|                          |               |                                                      |                                                                                                                                                                                                                                                                                                                                                             |
|--------------------------|---------------|------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>Revize 2 | June 20, 2025 | Revidováno na základě<br>dotazů NSAI pro<br>validaci | <input checked="" type="checkbox"/> Ano<br>Jazyk ověření: English<br><br><input type="checkbox"/> Ne (platí pouze u prostředků<br>třídy IIa nebo některých<br>implantovatelných prostředků<br>třídy IIb (MDR, článek 52 (4) 2.<br>odstavec), u kterých dosud není<br>ověřeno SSCP oznámeným<br>subjektem)<br><br><input type="checkbox"/> Jiné (upřesněte): |
|--------------------------|---------------|------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

## Resumé af sikkerhed og klinisk ydelse

### FemoSeal™ Vascular Closure System

|                                                  |                                                                                             |
|--------------------------------------------------|---------------------------------------------------------------------------------------------|
| <b>Produceret af</b>                             | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 USA         |
| <b>Producentens SRN</b>                          | US-MF-000019594                                                                             |
| <b>Management Representative/PRRC</b>            | Kimberly Feitl<br>Vice President, Quality                                                   |
| <b>Basic UDI-DI:</b>                             | 38970FS79                                                                                   |
| <b>EMDN-nummer</b>                               | C900199 – Hæmostasesystemer - Andet                                                         |
| <b>Udstyrsklasse</b>                             | Klasse III                                                                                  |
| <b>Det år, hvor enheden først blev CE-mærket</b> | 2005                                                                                        |
| <b>EU-repræsentant</b>                           | Terumo Europe N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgium<br>SRN: BE-AR-000001433 |
| <b>Bemyndiget organ</b>                          | NSAI<br>CE 0050                                                                             |

## Indholdsfortegnelse

|            |                                                                                                    |          |
|------------|----------------------------------------------------------------------------------------------------|----------|
| <b>1.0</b> | <b>Resumé til brugere/sundhedspersonale .....</b>                                                  | <b>5</b> |
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| 1.1.2      | Indikationer for brug.....                                                                         | 5        |
| 1.1.3      | Kontraindikationer og/eller begrænsninger .....                                                    | 5        |
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| 1.1.5      | Særlige patientpopulationer .....                                                                  | 5        |
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| 1.2.4      | Tidligere generation(er) eller varianter.....                                                      | 10       |
| 1.2.5      | Tilbehør, der er beregnet til brug sammen med anordningen.....                                     | 10       |
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| 1.3        | Risici og advarsler.....                                                                           | 10       |
| 1.3.1      | Resterende risici og bivirkninger .....                                                            | 10       |
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Formålet med dette resumé af sikkerhed og klinisk ydelse (SSCP) er at give offentlig adgang til et opdateret resumé af de vigtigste aspekter af sikkerhed og kliniske ydelse for FemoSeal™ Vascular Closure System (VCS).

**Afsnit 1.0** nedenfor indeholder et resumé af anordningens sikkerhed og kliniske ydeevne, beregnet til brugere/sundhedspersoner.

## **1.0 RESUMÉ TIL BRUGERE/SUNDHEDSPERSONALE**

SSCP'et er ikke beregnet til at erstatte brugsanvisningen som hoveddokument for at garantere sikker brug af enheden, og det er heller ikke beregnet til at give diagnostiske eller terapeutiske forslag til tilsigtede brugere eller patienter. SSCP'en er ikke beregnet til at erstatte de obligatoriske oplysninger på implantatkortene eller i andre obligatoriske dokumenter.

### **1.1 Tilsigtet brug af udstyret**

#### **1.1.1 Tilsigtet brug**

FemoSeal™ Vascular Closure System er en medicinsk anordning, der er beregnet til at lukke en arteriepunktur efter perkutan kateterisering gennem femoralarterien.

#### **1.1.2 Indikationer for brug**

FemoSeal™ Vascular Closure System er indiceret til lukning af en punktur af femoralarterien (arteriotomi) hos patienter, som har fået foretaget en perkutan kateterisation ved hjælp af et 7F (2,33 mm) eller mindre indføringshylster.

#### **1.1.3 Kontraindikationer og/eller begrænsninger**

FemoSeal™ Vascular Closure System er kontraindiceret til patienter med arteriotomier, hvor der er anvendt indføringshylstre eller anordninger større end 7F (2,33 mm).

#### **1.1.4 Tilsigtede patientpopulationer**

Sikkerheden og effektiviteten af FemoSeal™ Vascular Closure System er blevet fastslået hos patienter på 18 år og derover, som har fået foretaget perkutan kateterisation med et 7F (2,33 mm) eller mindre indføringshylster.

#### **1.1.5 Særlige patientpopulationer**

Sikkerhed og effektivitet af FemoSeal™ Vascular Closure System er ikke blevet fastslået hos følgende patientpopulationer:

- Patienter med eksisterende autoimmun sygdom.
- Patienter, der gennemgår terapeutisk trombolyse.
- Patienter med klinisk signifikant perifer vaskulær sygdom.
- Patienter med ukontrolleret hypertension (> 220 mmHg systolisk eller > 110 mmHg diastolisk).
- Patienter med blødningsforstyrrelser, herunder trombocytopeni (< 100.000 trombocytter/l) eller anæmi (Hgb < 10 mg/dl).



- Patienter med en indvendig lumen i femoralarterien, der er mindre end 5 mm.
- Patienter med nedsat nyre- og/eller leverfunktion.
- Patienter med anden relevant komorbiditet.
- Population med specifik racemæssig og/eller etnisk oprindelse.
- Patienter med myokardieinfarkt inden for 72 timer.
- Patienter med et vaskulært transplantat eller en stent på punkturstedet.
- Gravide eller ammende patienter.
- Patienter under 18 år.

### 1.1.6 Tilsigtede brugere

De tilsigtede brugere af FemoSeal™ Vascular Closure System er læger med en uddannelse, der kvalificerer dem til at udføre arteriel adgang og lukning i forbindelse med endovaskulære procedurer gennem femoralarterien, og som har deltaget i et Terumo Medical Corporations FemoSeal™ lægevejledningsprogram.

## 1.2 Produktbeskrivelse

### 1.2.1 Beskrivelse af produktet

FemoSeal™ Vascular Closure System, der er fremstillet af Terumo Medical Corporation (TMC), er en resorberbar vaskulær lukkeanordning, der er designet til at opnå femoral arteriel hæmostase efter perkutan kateterisering gennem femoralarterien.

FemoSeal™ lukkeelementer består af to resorberbare polymerskiver, den indvendige forsegling og den udvendige låseskive, som holdes sammen af et resorberbart multifilament, hvorved arteriotomien forsegles mekanisk (se **figur 1.1** og **figur 1.2**). Når den udvendige låseskive er anlagt via indføringssheathet, trykkes den fast på multifilamentskafte, hvilket resulterer i mekanisk lukning af punkturstedet mellem den indvendige og udvendige låseskive. Den indvendige forsegling og den udvendige låseskive holdes på plads via friktion på multifilamentakslen. Hæmostase opnås mekanisk. Lukkeelementerne nedbrydes ved hydrolyse.

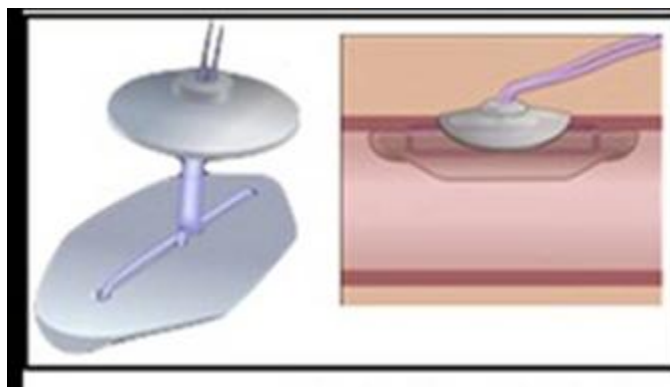
De implanterbare lukkekomponenter, den indvendige forsegling og den udvendige låseskive nedbrydes i løbet af atten (18) måneder, mens multifilamentet skønnes at være nedbrudt og absorberet ved hydrolyse af det omgivende væv efter to (2) til tre (3) år. De implanterbare lukkekomponenters evne til at opretholde kompression på arteriotomien er blevet testet i op til otte (8) timer. Nedbrydningsprodukterne metaboliseres og udskilles i urinen eller udskilles som kuldioxid via lungerne. Der er ikke observeret nogen akkumulerende virkninger i dyreforsøg. De

andre FemoSeal™-komponenter, der kommer i kontakt med levende væv eller blod under indgrebet, er indføringssheath, dilatator, stamper, skubber og guidewire.

**Figur 1.1** Henholdsvis indvendig forsegling og udvendig låseskive

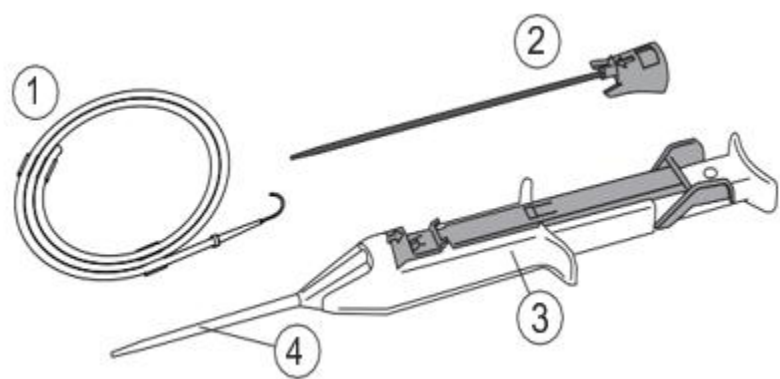


**Figur 1.2** Indvendig forsegling og udvendig låseskive anbragt



FemoSeal™-enheden er pakket sammen med en dilatator og en guidewire med en ydre diameter på 0,038" (0,97 mm) og en længde på 27,5" (70 cm) samt en J-spids, se **figur 1.3** nedenfor. Guidewiren er indkapslet i et polyethylenrør. Alle dele er pakket i en fast papirbakke. Pakningen indeholder desuden patientens implantatkort. FemoSeal™ Vascular Closure System kræver ikke yderligere tilbehør, for at enheden kan fungere efter hensigten, og enheden er kun beregnet til brug med dilatatorens og guidewiren, der er inkluderet i produktets emballage.

**Figur 1.3 FemoSeal™ Vascular Closure System med guidewire og dilatator**



**1.2.2 Råmaterialer og komponenter**

Tabel 1.1 nedenfor viser komponenterne i FemoSeal™ VCS.

**Tabel 1.1 FemoSeal™ VCS Råmaterialer og komponenter**

| Reservedelsnummer | Beskrivelse                            |                                                             | Materialer                                                                                                                                                                           |
|-------------------|----------------------------------------|-------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1                 | 0,038" (0,97 mm) guidewire med J-spids |                                                             | Guidewire: 304 Rustfrit stål<br><br>J-spids: Polypropylen, lilla pigment<br><br>Klemme: Polyetylen<br><br>Slange: Polyetylen                                                         |
| 2                 | FemoSeal Dilatator                     |                                                             | Krave: Tetrahydrofuran, blåt pigment, polybutylenterephthalat (PBT)<br><br>Rør: Polyethylen med høj densitet (HDPE), sort pigment<br><br>Smøremiddel: Silikone Dow Corning 360       |
| 3/4               | FemoSeal enhed                         | Formstøbt RD7 – indvendig forsegling og udvendig låseskive* | Copolymer mellem glycolid, trimethylencarbonat, ε-caprolacton og TMP: trimethylolpropan (initiator)                                                                                  |
|                   |                                        | Multifilament*                                              | Segmenteret copolymer mellem L,L-lactid, trimethylencarbonat, ε-caprolacton og 1,3 propanediol (initiator)<br><br>Belægningen er copolymer mellem glycolid, ε-caprolacton og L-lysin |

|  |  |                         |                                                 |
|--|--|-------------------------|-------------------------------------------------|
|  |  | Stamper                 | Polypropylen                                    |
|  |  | Skubber                 | 304V Rustfrit stål                              |
|  |  | Glider                  | Polybutylenterephthalat (PBT)                   |
|  |  | Indkapsling             | Polybutylenterephthalat (PBT)                   |
|  |  | Knap                    | Polybutylenterephthalat (PBT)                   |
|  |  | Knaplåg                 | Polyoxymethylen (POM)/polyacetal-copolymer      |
|  |  | Sleeve                  | Polybutylenterephthalat (PBT)                   |
|  |  | Afstandsstykke          | Polybutylenterephthalat (PBT)                   |
|  |  | Kegle                   | Polypropylen                                    |
|  |  | Låg på indkapsling      | Polybutylenterephthalat (PBT)                   |
|  |  | Sikkerhedslås           | Polybutylenterephthalat (PBT), blåt pigment     |
|  |  | Låg til sleeve          | Polybutylenterephthalat (PBT)                   |
|  |  | Rørpakning              | Silikone hårdhed A 70                           |
|  |  | Pakning til indkapsling | Silikone hårdhed A 50                           |
|  |  | Fjeder                  | 302 Rustfrit stål                               |
|  |  | Indføringsseath         | Polypropylen<br>Silikone Dow Corning 360, hexan |

\* Implanterbar del af anordningen; implanterbare komponenter er MR-sikre

FemoSeal™ VCS er steriliseret med ethylenoxid (EO) og er medicinsk udstyr til engangsbrug. FemoSeal™ VCS-enheden er konstrueret på en sådan måde, at den ikke kan genbruges.

### **Virkningsmekanisme**

FemoSeal™ Vascular Closure System fremmer mekanisk hæmostase ved at anbringe implanterbare lukkeelementer inde i og uden for femoralarterien. Mekanismen, der forebygger blødning, leveres af den indvendige forsegling, som forsegler punkturstedet, og den udvendige låseskive, der holder den indvendige forsegling på plads.

#### **1.2.3 Klinisk fordel**

FemoSeal™ Vascular Closure System giver følgende kliniske fordele i forhold til lukning af blodkar efter punktur af femoralarterien:

- Reduceret tid indtil hæmostase <sup>1</sup>
- Reduceret tid indtil patienten er mobil <sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

#### 1.2.4 Tidligere generation(er) eller varianter

- Den første version af FemoSeal™ Vascular Closure System (#11200) blev solgt på det europæiske marked i 2005 og en del af 2006.
- Det nuværende FemoSeal™ Vascular Closure System (#11202) med et forbedret applikationssystem har været på markedet siden 28. marts 2006.

#### 1.2.5 Tilbehør, der er beregnet til brug sammen med anordningen

FemoSeal™-enheden er pakket sammen med en dilatator, en guidewire med en ydre diameter på 0,038" (0,97 mm), en længde på 27,5" (70 cm) og en J-spids. Guidewiren er tilbehør til FemoSeal™-enheden. J-spidsen er en komponent til guidewiren, mens dilatatoren er en komponent til FemoSeal™-enheden. Guidewiren er det eneste, der regnes som tilbehør. Guidewiren er indkapslet i et polyethylenrør. Alle dele er pakket i en fast papirbakke. Pakningen indeholder desuden patientens implantatkort. FemoSeal™ Vascular Closure System kræver ikke yderligere tilbehør, for at enheden kan fungere efter hensigten, og enheden er kun beregnet til brug med dilatatoren og guidewiren, der er inkluderet i produktets emballage.

#### 1.2.6 Andre anordninger og produkter, der er beregnet til at blive brugt i kombination med udstyret

FemoSeal™ Vascular Closure System kræver ikke yderligere udstyr for at fungere efter hensigten.

### 1.3 Risici og advarsler

#### 1.3.1 Resterende risici og bivirkninger

Kendte eller forudsigelige utilsigtede hændelser, skader og komplikationer i forbindelse med brug af FemoSeal™ VCS som følge af resterende risici er anført i **tabel 1.2**.

Forekomsthypigheden er baseret på en analyse af risikodokumentationen og beregnet på baggrund af data fra overvågning efter markedsføringen fra 1. September 2019 til og med 31. August 2024. Der er ingen ukendte resterende risici for FemoSeal™ VCS, og alle relevante risici er blevet håndteret gennem brugsanvisningen og risikostyringsprocessen.

**Tabel 1.2. FemoSeal utilsigtede hændelser/komplikationer**

| Skade                                     | Incidenshyppighed (%) | Afbødende faktorer                                                                                                                                                         |
|-------------------------------------------|-----------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Allergisk reaktion                        | 0,0000                | Handlinger og planer for at reducere risikoen mest muligt er blevet håndteret med produktdesignfunktioner, fremstillingsretningslinjer, produktmærkning og lægeuddannelse. |
| Aneurisme                                 | 0,0000                |                                                                                                                                                                            |
| AV-fistel                                 | 0,0001                |                                                                                                                                                                            |
| Blodtab/blødning                          | 0,0280                |                                                                                                                                                                            |
| Død                                       | 0,0002                |                                                                                                                                                                            |
| Ekkymose                                  | 0,0000                |                                                                                                                                                                            |
| Emboli                                    | 0,0000                |                                                                                                                                                                            |
| Reaktion på fremmedlegemer                | 0,0000                |                                                                                                                                                                            |
| Hæmatom                                   | 0,0027                |                                                                                                                                                                            |
| Blødning                                  | 0,0001                |                                                                                                                                                                            |
| Infektion                                 | 0,0002                |                                                                                                                                                                            |
| Inflammatorisk reaktion                   | 0,0000                |                                                                                                                                                                            |
| Følelsesløshed                            | 0,0000                |                                                                                                                                                                            |
| Smerter                                   | 0,0000                |                                                                                                                                                                            |
| Ubehag for patienten                      | 0,0004                |                                                                                                                                                                            |
| Procedureforsinkelse                      | 0,0065                |                                                                                                                                                                            |
| Pseudoaneurisme                           | 0,0004                |                                                                                                                                                                            |
| Retroperitoneal blødning                  | 0,0002                |                                                                                                                                                                            |
| Sepsis                                    | 0,0000                |                                                                                                                                                                            |
| Tromboemboli                              | 0,0000                |                                                                                                                                                                            |
| Trombose                                  | 0,0001                |                                                                                                                                                                            |
| Karokklusion/iskæmi i nedre ekstremiteter | 0,0002                |                                                                                                                                                                            |
| Perforering af kar                        | 0,0000                |                                                                                                                                                                            |
| Dissektion/laceration af karvæv           | 0,0003                |                                                                                                                                                                            |

### 1.3.2 Advarsler og forholdsregler

#### Advarsler

1. Må ikke anvendes, hvis emballagen er beskadiget, eller en steril barriere ikke er intakt.
2. Må ikke anvendes efter udløbsdatoen – de biologisk nedbrydelige komponenter fungerer muligvis ikke korrekt.
3. Må ikke anvendes, hvis nogen af delene ser ud til at være beskadigede eller defekte på nogen måde.
4. Brug af FemoSeal™ Vascular Closure System, hvor der kan være opstået bakteriel kontaminering af indføringssheathet eller det omgivende væv, kan forårsage infektion.
5. Hvis der er mistanke om, at den posteriore arterievæg er punkteret, eller der er foretaget mere end én arteriepunktur, må man ikke udelukkende stole på, at FemoSeal™ Vascular Closure System kan give arteriel hæmostase. Brug yderligere manuel eller mekanisk kompression.
6. Hvis punkturstedet er i eller distalt for femoralisarteriens bifurkation, må FemoSeal™ Vascular Closure System ikke anvendes, da der er risiko for, at den indvendige forsegling kan blive anbragt forkert. Denne hændelse kan medføre blødningskomplikationer og/eller afbrydelse af den normale blodgennemstrømning.
7. Hvis der er vedvarende arteriel blødning fra incisionsstedet, må multifilamentet ikke klippes, før der er opnået hæmostase. Hvis der ikke opnås hæmostase, skal multifilamentet fastgøres med en steril sårbandage, og der skal anvendes supplerende kompression, indtil der opnås hæmostase. I tilfælde af vedvarende arteriel blødning kan der opstå signifikante blødningskomplikationer, som kan resultere i skade på patienten, eller at denne dør.
8. FemoSeal™ Vascular Closure System må ikke anvendes, hvis punkturstedet er proksimalt for det ingvinale ligament, da dette kan resultere i et retroperitonealt hæmatom.
9. Patienter med en højere risiko for blødning kan opleve øget blodtab, hvilket kræver transfusion.
10. Hvis den indvendige skive løsner sig, kan det potentielt forårsage en trombotisk og/eller embolisk hændelse.

#### Forholdsregler

1. FemoSeal™ Vascular Closure System skal anlægges af læger med tilstrækkelig uddannelse i brugen af anordningen.

2. Der skal udføres et begrænset femoralt angiogram eller en ultralydsvejledt punktur af femoralarterien inden anlæggelse af FemoSeal™ Vascular Closure System.
3. Afbryd proceduren, hvis:
  - Lumendiameter af femoralarterien < 5 mm.
  - Stenose og/eller betydelig plaque i området omkring punkturstedet ved femoralarterien.
  - Arteriepunktur er ved eller distalt for bifurkationen af femoralarterien.
  - Der er abnorme grene eller karabnormiteter i området omkring punkturstedet ved femoralarterien.
4. Hvis der er hæmatomer til stede, skal der udvises ekstra forsigtighed for at sikre korrekt indføring af indføringssheathet i arterien.
5. Brug en punkturteknik, der gennembryder én væg. Arteriens bageste væg må ikke punkteres.
6. Følg altid steril teknik ved brug af FemoSeal™ Vascular Closure System.
7. FemoSeal™ Vascular Closure System er kun til engangsbrug og må ikke resteriliseres eller genanvendes på nogen måde. FemoSeal™-enheden er konstrueret således, at den ikke kan genanvendes.
8. Afbryd proceduren, hvis placeringen af den indvendige forsegling møder uventet modstand.
9. For korrekt placering af den indvendige forsegling skal tommelfingeren flyttes, så knappen frit kan springe tilbage.
10. Sørg for, at spidsen af FemoSeal™-anordningens indføringssheath er under hudens overflade, inden den udvendige låseskive placeres. Den udvendige låseskive kan uforvarende blive anbragt over hudniveau hos patienter, der har kort afstand mellem femoralarterien og hudniveauet.
11. Det kan være nødvendigt med en hudincision før anlæggelse for at opnå en korrekt placering.
12. Hvis den indvendige forsegling er inde i arterien, men det ikke kan lade sig gøre at trykke knappen helt ned og anbringe den udvendige låseskive, kan det være nødvendigt med et kirurgisk indgreb for at fjerne FemoSeal™ lukkeelementerne.
13. Hvis det bliver nødvendigt at foretage en ny punktur af den samme femoralarterie inden for 18 måneder, skal den nye punktur foretages mindst én centimeter proksimalt for det tidligere punktursted for FemoSeal™ Vascular Closure System.



14. Instruer patienten i at følge lægens anvisninger vedrørende inspektion af lukningsstedet.

15. Bed patienten om at have patientinformationskortet på sig i de næste 18 måneder

### **Forholdsregler ved udskrivning**

Inden udskrivning overvejes, skal patienten vurderes for følgende kliniske tilstande:

1. Blødning og/eller hæmatom ved lukningsstedet.
2. Smerter ved gang.
3. Tegn på infektion ved lukningsstedet.

### **1.3.3 Sikkerhedsrelaterede korrigerende handlinger**

Der var én sikkerhedsrelateret korrigerende handling, der involverede FemoSeal™ VCS, i perioden fra 1. september 2019 til og med 31. august 2024.

I 2022 tilbagekaldte Terumo frivilligt FemoSeal™ VCS på grund af klager over fejl i proces- og batchfrigivelsestest af Elkton-producerede FemoSeal-produkter til måling af kompressionskraft og tilbagetrækningskraft. I alt blev 950 enheder tilbagekaldt fra Sydkorea.

## **1.4 Klinisk evaluering og klinisk opfølgning efter markedsføring**

**Tabel 1.3** indeholder en liste over pivotale forsøg, der er inkluderet med henblik på markedsføringen af FemoSeal™ VCS samt forsøg efter markedsføring og kliniske opfølgningsaktiviteter efter markedsføring. Den version af udstyret, der anvendes i forsøget, er inkluderet i tabellen nedenfor. Den første version af FemoSeal™ VCS (#11200) var på markedet indtil 2006, mens den næste version (#C11202) blev lanceret på markedet i 2006 og er den, der er på markedet i dag.

**Tabel 1.3 Oversigt over pivotale forsøg**

| <b>Funktionstest på dyr før markedsføring</b>                                                                                                                                                                                                                           | <b>Version af udstyret</b> |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                      |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                      |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                      |
| <b>Første kliniske forsøg med mennesker</b>                                                                                                                                                                                                                             |                            |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                      |

| Gennemførte kliniske forsøg efter markedsføring                                                                                 |                          |
|---------------------------------------------------------------------------------------------------------------------------------|--------------------------|
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                      | C11202<br>(aktuel enhed) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                               | C11202<br>(aktuel enhed) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | C11202<br>(aktuel enhed) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)          | C11202<br>(aktuel enhed) |
| Planlagte/igangværende kliniske forsøg efter markedsføring                                                                      |                          |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                      | C11202<br>(aktuel enhed) |
| Kliniske opfølgningsaktiviteter efter markedsføring                                                                             |                          |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(aktuel enhed) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(aktuel enhed) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(aktuel enhed) |

#### 1.4.1 Resumé af data (fra dyreforsøg og kliniske forsøg) før markedsføring

Tabel 1.4 nedenfor beskriver alle forsøg før markedsføring, både dyreforsøg og kliniske forsøg.

**Tabel 1.4 Opsummeringer af forsøg før markedsføring**

| Funktionstest på dyr før markedsføring                                                                                                                                                                                                                                  |                                                                   |                                      |                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------|--------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Forsøgets navn                                                                                                                                                                                                                                                          | År / CI                                                           | Forsøgstype                          | Formål                                                                                                                                                                                                                                          | Delmål                                                                                                                                                                                                                                                                                                                                                         | Potentielle godkendelseskriterier                                                                                                                                                                                                                                                                                                                                                                                                |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 2000<br>Radi Medical System AB<br><br>Udført af Biomatech, France | Dyreforsøg; Eksplorativ undersøgelse | Formålet med forsøget var at vurdere biokompatibiliteten og biofunktionaliteten af et bionedbrydeligt implantat, designet til at opnå hæmostase i det vaskulære system. Rapporten omhandler reservedyr fra forsøg nr. 862 (dokumentnr. 1051-01) | N = 3 voksne hunfår, 1 dyr pr. tidspunkt<br><br>Opfølgning med henblik på histopatologisk analyse, makroskopisk klassifikation og ultrastrukturel analyse<br><br><ul style="list-style-type: none"> <li>12 mdr.</li> <li>15 mdr.</li> <li>18 mdr.</li> </ul><br>Farve-Doppler ultralydsopfølgning – 30 dage på adgangsstederne i halspulsåre og femoralarterie | Arteriel åbenhed <ul style="list-style-type: none"> <li>Vurdering af blodgennemstrømning efter anlæggelse – 2/3 reduktion af blodgennemstrømning i forbindelse med midlertidig arteriel vasospasme, som blev tilskrevet proceduren, begge forekom ved venstre femoralarterie</li> <li>Farve-Doppler ultralydsvurdering (4 uger) – 3/3 (100 %) uden større reduktion af blodgennemstrømning 30 dage efter implantation</li> </ul> |

|  |  |  |  |  | <p>Makroskopiske observationer</p> <ul style="list-style-type: none"> <li>12 måneder – åbenhed bekræftet makroskopisk ved fravær af anatomisk synlig okklusion; ingen makroskopiske lokale intolerancelæsioner (blødning, nekrose eller neovaskularisering); indkapsling af intern skive syntes at være markeret</li> <li>15 måneder – makroskopisk observation viste ingen tegn på inflammation; ingen rester af indvendige eller udvendige skiver identificeret; indkapslingsvæv i området for den udvendige skive så ud som ved observationen efter 12 måneder</li> <li>18 måneder – makroskopisk observation viste ingen tegn på lokal intolerance, udvendig skive synlig (3/3 tilfælde), nedbrydning af indvendig skive komplet; 1/3 (venstre halspulsåre) - depression af arterievæggen observeret ved implantationsstedet (kan være relateret til anbringelse af anordningen)</li> </ul> <p>Konklusion</p> <ul style="list-style-type: none"> <li>Makroskopisk blev der ikke påvist nekrotiske, degenerative eller trombotiske tegn 12, 15 og 18 måneder efter implantationen.</li> <li>Nedbrydningsprocessen af de indvendige og udvendige skiver syntes at avancere mellem 12 og 18 måneder og er helt sammenføjet efter 18 måneder med et hvidligt væv, der dækkede det implanterede område.</li> <li>Histologisk var polymermateriale ikke længere synligt efter 18 måneder, men endoluminalt fibrøst væv var til stede. Der blev ikke observeret nekrotiske, degenerative eller trombotiske læsioner.</li> </ul> |
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| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002 Radi Medical System AB</p> <p>Udført af Biomatech, France</p> | <p>Dyreforsøg; Eksplorativ undersøgelse</p> | <p>Formålet med forsøget var at vurdere biokompatibiliteten og biofunktionaliteten af et bionedbrydeligt implantat, designet til at opnå hæmostase i det vaskulære system.</p> | <p>Opfølgning (efter implantation)</p> <ul style="list-style-type: none"> <li>• 12 uger</li> <li>• 24 uger</li> <li>• 36 uger</li> </ul> <p>N = 12 får, 3 dyr pr. tidspunkt, 3 reservedyr opgivet ved 12, 15 og 18 måneder</p> <p>Implantationssteder – højre og venstre femoralarterie højre og venstre halspulsåre</p> <p>Farve-Doppler ultralydsanalyse</p> | <p><u>Åbenhed i halspulsåre og femoralarterie efter 4 uger</u></p> <ul style="list-style-type: none"> <li>• Større reduktion af blodgennemstrømningen 0/12 (0 %)</li> </ul> <p><u>Ingen større reduktion af blodgennemstrømningen</u></p> <ul style="list-style-type: none"> <li>• Svært nedsat blodgennemstrømning i forbindelse med indføring af anordningen 0/12 (0 %)</li> <li>• Reduktion i blodgennemstrømning i venstre halspulsåre 2/12 (16,6 %) på grund af midlertidig arteriel vasospasme (tilskrevet operation, ikke enheden)</li> </ul> <p><u>Nedsat blodgennemstrømning ved opfølgning</u></p> <p>12 uger – 0/12 (0 %)</p> <p>24 uger – 0/12 (0 %)</p> <p>36 uger – 0/12 (0 %)</p> <p>Blodtryksmålinger (3 får – 36 uger)</p> <ul style="list-style-type: none"> <li>• Ingen større reduktion i blodgennemstrømningen detekteret</li> </ul> <p>Makroskopiske data til integration og nedbrydning (grad 0-4)</p> <p><u>Adgang via halspulsåre</u></p> <p><u>Indvendig side</u></p> <p>-indkapsling</p> <p>12 uger 1,3</p> <p>24 uger 0,8</p> <p>36 uger 0,7</p> <p>-materialenedbrydning</p> <p>12 uger 2,2</p> <p>24 uger 2,3</p> <p>36 uger 0,7</p> <p><u>Udvendig side</u></p> <p>-indkapsling</p> <p>12 uger 2,0</p> <p>24 uger 1,0</p> <p>36 uger 0,8</p> <p>-materialenedbrydning</p> |
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|  |  |  |  |  | 12 uger 2,0<br>24 uger 2,7<br>36 uger 3,2<br><br><i>Femoral adgang</i><br><i>Udvendig side</i><br>-indkapsling<br>12 uger 1,0<br>24 uger 2,7<br>36 uger 1,0<br>-materialenedbrydning<br>12 uger 2,0<br>24 uger 2,4<br>36 uger 3,0<br><br><i>Indvendig side</i><br>-indkapsling<br>12 uger 2,0<br>24 uger 1,2<br>36 uger 1,0<br>-materialenedbrydning<br>12 uger 1,0<br>24 uger 2,2<br>36 uger 3,0<br><br><u>Histologiske data for<br/>integration, nedbrydning og<br/>inflammatoriske parametre<br/>(gennemsnit af relevante<br/>værdier, indeks 0-4) n=6</u><br><br><u>Adgang via halspulsåre</u><br>Ekstern fibrose<br>12 uger – 2,3<br>24 uger – 2,3<br>36 uger – 1,8<br>Indvendig neointima<br>12 uger – 3,0<br>24 uger – 2,7<br>36 uger – 3,3<br>Materialenedbrydning<br>12 uger – 1,7<br>24 uger – 3,0<br>36 uger – 3 +<br>Inflammatoriske parametre<br>(makrofager)<br>12 uger – 3,0<br>24 uger – 1,7<br>36 uger – 1,7<br><br><i>Femoral adgang</i><br>Ekstern fibrose |
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|  |  |  |  |  | 12 uger – 1,3<br>24 uger – 1,5<br>36 uger – 1,7<br>Indvendig neointima<br>12 uger – 3,7<br>24 uger – 3,3<br>36 uger – 3,8<br>Materialenedbrydning<br>12 uger – 2,0<br>24 uger – 3,0<br>36 uger – 3+<br>Inflammatoriske parametre<br>(makrofager)<br>12 uger – 3,5<br>24 uger – 1,8<br>36 uger – 1,8<br><br><u>Histomorfologiske<br/> åbenhedsværdier</u><br>Adgang via halspulsåre<br>12 uger 74,0 %<br>24 uger 81,9%<br>36 uger -89,43 %<br>Femoral adgang<br>12 uger – 42,2%<br>24 uger – 73,21%<br>36 uger – 78,71 %<br><br><u>Ultralyd vaskulær åbenhed<br/> (middel %)</u><br>Adgang via halspusåre<br>12 uger 94,6%<br>24 uger – 96,7%<br>36 uger – 94,7%<br>Femoral adgang<br>12 uger – 66,9%<br>24 uger – 63,6%<br>36 uger – 75,1%<br><br>Konklusion <ul style="list-style-type: none"> <li>• Der blev ikke påvist noget signifikant tegn på lokal intolerance (fravær af synlige inflammatoriske, nekrotiske eller degenerative læsioner) efter 12, 24 eller 36 uger</li> <li>• Ingen signifikant uønsket vævsreaktion registreret med hensyn til vært og enhed</li> <li>• Nedbrydningen af implantatet var næsten fuldført efter 36 uger</li> </ul> |
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|                                                                                                                                                                                                                                                                 |                                                                       |            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
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| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France). | 2002<br><br>Radi Medical System AB<br><br>Udført af Biomatech, France | Dyreforsøg | Formålet med forsøget var at vurdere biokompatibiliteten og biofunktionaliteten af et bionedbrydeligt implantat, designet til at opnå hæmostase i det vaskulære system. Det afprøvede produkt var beregnet til at gå ind i punkturhullet i arterierne for at opnå hæmostase. Den ene skive kom ind i punkturhullet i arterien, og den anden strammede den indvendige skive fra ydersiden af arterien. Begge skiver blev indført gennem et introducersheath. Skiverne var designet til at forhindre blødning, til at hele ind i karvæggen og til sidst nedbrydes og absorberes. Forsøget var designet til at indsamle og analysere data efter funktionel implantation hos får og grise for at evaluere implantatets evne til at opretholde den fysiologiske funktion, når det anvendes i kredsløbssystemet, med henblik på at bestemme værtens respons og implantatets respons (fysisk integritet, vævsindkapsling ved okklusion) og for at evaluere nedbrydningen af implantatet | Implantationsperiode/opfølgning er 5 uger for alle dyr<br><br>4 får, 1 gris<br><br>14 lukkeelementer<br><br>8 lukkeelementer implanteret i 2 får,<br><br>2 lukkeelementer implanteret i 1 gris<br><br>Da to lukkeelementer blev implanteret i samme femoralarterie, blev de implanteret i en afstand > 30 mm | Alle kriterier for uønskede tegn (inflammation, nekrose, blødning eller enhver anden læsion) eller enhver form for tynd pseudo-intimal lagdannelse blev registreret. Der blev lagt særlig vægt på den indledende vævsintegration af anordningen med særlig vægt på den indvendige indkapsling af skiven.<br><br>Makroskopisk blev der ikke observeret nogen signifikante tegn på lokal intolerance eller trombedannelse. Den makroskopiske observation afslørede ingen forskel mellem fårene eller grisen efter implantation af lukkeelementerne i femoralarterien. Makroskopisk blev der ikke observeret nogen signifikante tegn på lokal intolerance eller trombedannelse. Den makroskopiske observation afslørede ingen forskel mellem fårene eller grisen efter implantation af lukkeelementerne i femoralarterien.<br><br>Den histopatologiske analyse af implantationsstedet hos får viste ingen lokale bivirkninger. De indvendige og udvendige skiver viste tegn på nedbrydning og var i nogle tilfælde nedbrudt i mindre dele. De indvendige skiver blev fuldstændig integreret i neointimalt væv. Hos grisen viste den histopatologiske analyse lidt flere inflammatoriske tegn |
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|                                                                                                                                                                                                              |                              |                                      |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                          | <p>omkring den indvendige og udvendige skive. Hos begge dyr udviste multifilamentet lidt flere inflammatoriske tegn end i skivematerialet, hvilket er normalt for flettede suturer på grund af det større overfladeareal.</p> <p>Karpassagen blev målt efter 5 uger ved hjælp af tre forskellige metoder, histomorfometrisk, histomorfometrisk i kombination med måling af kardiameter ved hjælp af skydelære og ved brug af farve-Doppler-ultrasonografi. Den gennemsnitlige vaskulære åbenhed hos får var mellem 60 og 80 % afhængigt af metoden (12 observationer). Hos grisen var den gennemsnitlige åbenhed mellem 40 og 80 % (2 observationer).</p> |
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| <b>Første kliniske forsøg med mennesker</b>                                                                                                                                                                  |                              |                                      |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| <b>Forsøgets navn</b>                                                                                                                                                                                        | <b>År / CI</b>               | <b>Forsøgstype</b>                   | <b>Formål</b>                                                                                                                                                                                                                                                                                            | <b>Delmål</b>                                                                                                                                                                                                                                                                                            | <b>Potentielle godkendelseskriterier</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Åbent, enkeltarmet multicenterforsøg | Formålet med forsøget var at bestemme sikkerheden, ydeevnen og effektiviteten af FemoSeal Vascular Closure System (FemoSeal System) generelt og især lukkeelementerne hos patienter, der gennemgik hjertediagnostiske eller interventionelle kardiologiske procedurer via adgang gennem femoralarterien. | 2-delt forsøg<br>Total n = 80<br>Del 1 n = 20<br>Del 2 n = 60<br>Indikationer:<br>Del 1 – diagnostisk hjertekateterisering ved brug af femoralarterien som adgangssted<br><br>Del 2 – patienter, der gennemgår diagnostiske og interventionelle kardielle procedurer med femoralarterien som adgangssted | Resultater<br>- <u>hæmostase opnået med FS uden kompression</u><br>- Del 1 20/20 (100 %)<br>- Del 2 58/60 (97 %)<br>Mediantid til hæmostase på tidspunktet for proceduren (Del 2) - 1,0 minut (omgående interval – 8 minutter)<br><br><u>Tid til patienten var mobil (minutter)</u><br>Del 1 - median: 33,0<br>middelværdi: 67,8<br>Del 2 -                                                                                                                                                                                                                                                                                                               |



|  |  |  |  | 30 dages opfølgning | median: 45<br>middelværdi: 87,5<br><br><u>Forekomst af større vaskulære komplikationer – 30-dages opfølgning</u><br>Del 1<br>-Fri for vaskulære komplikationer 20/20 (100 %)<br>Del 2<br>Pseudoaneurisme – 1/59 (1,69 %)<br><br><u>Behandlingssvigt</u><br>Del 1 – 0/20 (0 %)<br>Del 2 – 3/60 (5 %) <ul style="list-style-type: none"> <li>2 på grund af manglende opnåelse af hæmostase uden brug af kompression</li> <li>1 på grund af større vaskulær komplikation, pseudoaneurisme</li> </ul><br><u>Vedvarende udsivning</u><br>Del 1 – 0/20 (0 %)<br>Del 2- 8/60 (13 %)<br><br><u>Hæmatom</u><br>Del 1 – 0/20 (0 %)<br>Del 2 – 6/60 (10 %) |
|--|--|--|--|---------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Som en del af udviklingsplanen for FemoSeal™ VCS før markedsføring blev der gennemført 3 funktionelle dyreforsøg. I 2000, før der blev indledt kliniske forsøg, blev der udført et dyreforsøg for at vurdere biofunktionaliteten af FemoSeal™ VCS. I dette forsøg vurderedes lukkeelementernes evne til at opretholde den fysiologiske funktion og evaluere deres nedbrydning. Efter 18 måneder var det indvendige og udvendige skivemateriale ikke længere synligt, efter at det var blevet erstattet med endoluminalt fibrøst væv. Konkluderende blev det bekræftet, at FemoSeal™ VCS lukkeelementet kan opretholde den fysiologiske funktion, når det anvendes i kredsløbssystemet.

I 2002 blev der udført et dyreforsøg for at vurdere biokompatibiliteten og biofunktionaliteten af et bionedbrydeligt implantat, FemoSeal™ VCS, der er designet til at opnå hæmostase i det vaskulære system. Sammenfattende var nedbrydningen af implantatet næsten fuldstændig efter 36 uger, og der var ingen signifikant uønsket vævsreaktion.

Et andet dyreforsøg i 2002 vurderede biokompatibiliteten og biofunktionaliteten af et bionedbrydeligt implantat, FemoSeal™ VCS, der er designet til at opnå hæmostase i det vaskulære system. Efter 5 uger var indkapslingen af skiven komplet, og tegn på nedbrydning blev observeret for indvendige og udvendige skiver. Afslutningsvis blev implantatets evne til at opretholde den fysiologiske funktion, når det anvendes i kredsløbssystemet, bekræftet.

Som en del af den kliniske udviklingsplan for FemoSeal™ VCS gennemførte Radi Medical System AB en klinisk undersøgelse før markedsføringen. Denne kliniske undersøgelse er ikke publiceret eller tilgængelig online. Forsøget med model #11200 blev udført i 2002-2004 i henhold til den europæiske standard EN 540 (Clinical Investigation of Medical Devices for Human Subjects) og i overensstemmelse med ICH General Considerations for Clinical Trials and Guideline for Good Clinical Practice. Detaljerne i dette forsøg er dokumenteret i rapport EU-SE-001. Det kliniske forsøg blev dokumenteret i den endelige rapport fra Radi Medical Systems AB, "Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures". Det kliniske forsøg blev udført med FemoSeal™s første model #11200 og fokuserede på sikkerheden og effektiviteten af de implanterbare lukkekomponenter. Den eneste forskel på den første model nr. 11200 og den nuværende model, C11202, er størrelsen, henholdsvis 6F og 7F, og det forbedrede applikationssystem. De kliniske fordele, den tilsigtede anvendelse, anvendelsesprincipperne og råmaterialerne til de implanterbare lukkeelementer, den indvendige forsegling og den udvendige låseskive forbliver uændrede.

Den tilsigtede anvendelse af enheden var til patienter, der gennemgik hjertediagnostiske eller interventionelle kardiologiske procedurer, hvor femoralarterien blev brugt som adgangspunkt. Formålet med dette forsøg var at bestemme sikkerheden, ydeevnen og effektiviteten af FemoSeal™ VCS. Dette var et prospektivt, åbent enkeltarmet multicenterforsøg med 30 dages opfølgning.

Det primære effektendepunkt var tid til hæmostase defineret som fravær af kraftig blødning. Det primære sikkerhedsendepunkt var forekomsten af større vaskulære komplikationer inden for 30 dage. Sekundære endepunkter omfattede tiden indtil patienten kunne gå, andel af behandlingssvigt, forekomst af uønskede hændelser og karakteristika for enhedens ydeevne under applikation og placering.

De patienter, der deltog i dette forsøg, var voksne, der var i stand til at afgive informeret samtykke og med mindst én intakt fodpuls. Patienterne blev ekskluderet fra forsøget, hvis de havde en eller flere af følgende tilstande:

- Perifer vaskulær sygdom i anamnesen
- Autoimmun sygdom
- Kendt blødningslidelse med svær anæmi
- INR >1,5
- Myokardieinfarkt inden for 72 timer
- Ukontrolleret hypertension på trods af behandling
- Fedme, der udelukker adgang med Seldinger-teknik
- Tilstedeværelse af vaskulær graft eller stent på arteriotomistedet
- Tidligere ipsilateral punktur inden for 3 måneder
- Forventet levetid < 6 måneder

Derudover blev patienterne undersøgt intraoperativt og udelukket fra forsøget, hvis et eller flere af følgende blev observeret:

- Lumendiameter af femoralarterien < 5 mm
- Arteriegrene inden for 2 cm proksimalt for punkturstedet
- Signifikant stenose inden for 3 cm fra punkturstedet
- Anvendelse af originalt indføringshylster > 6Fr
- Punktur ved eller distalt for bifurkation af femoralarterien
- Flere punkturer i femoralarterien
- Kendt eller formodet punktur af bagvæg i femoralarterien
- Stort hæmatom (2:6 cm) ved afslutningen af proceduren
- Vanskelig indføring af originalt indføringshylster for proceduren på grund af snoet væv eller kar

Dette enkeltprotokolforsøg blev udført i to dele: 20 patienter blev inkluderet i Del 1, hvorefter der blev gennemført en sikkerhedsanalyse, og derefter blev der inkluderet yderligere 60 patienter i Del 2.

I Del 1 var gennemsnitsalderen for inkluderede patienter 65,9 år, 70,0 % af patienterne var mænd, og 95 % af patienterne fik samtidig medicin. I Del 2 var gennemsnitsalderen 63,8 år, 78 % var mænd, og 100 % fik samtidig medicin.

Patienter, der gennemgik diagnostiske (Del 1 og Del 2) eller interventionelle (Del 2) hjertekateteriseringer, var egnede til inklusion i forsøget. Procedurene var i overensstemmelse

med standardbehandlingen på hvert af de inkluderede hospitaler efterfulgt af brugen af FemoSeal™ VCS. Patientdata blev indsamlet ved baseline, under proceduren og 1 dag og 30 dage efter proceduren. Resultaterne er opsummeret i **Tabel 1.5** og viser, at FemoSeal™ VCS er sikker og effektiv til brug i denne patientpopulation.

**Tabel 1.5 Kliniske resultater rapporteret i forsøget før markedsføring**

|                                                                                                                 | Del 1         | Del 2                      |
|-----------------------------------------------------------------------------------------------------------------|---------------|----------------------------|
| Antal patienter                                                                                                 | 20            | 60                         |
| Gennemsnitlig tid til hæmostase                                                                                 | 1,2 minutter  | 1,6 minutter <sup>a</sup>  |
| Gennemsnitlig tid til patienten var mobil                                                                       | 72,2 minutter | 87,5 minutter <sup>b</sup> |
| Incidens af større vaskulære komplikationer <sup>c</sup>                                                        | 0 (0 %)       | 1 (2 %)                    |
| Antal patienter med uønskede hændelser                                                                          | 5 (25 %)      | 19 (32 %)                  |
| Behandlingssvigt (defineret som større vaskulære komplikationer, behov for manuel kompression eller begge dele) | 0 (0 %)       | 3 (5 %)                    |
| Funktionsfejl på udstyret                                                                                       | 0 (0 %)       | 6 (10 %)                   |

<sup>a</sup> Baseret på en samlet forsøgsstørrelse på 58, fordi 2 forsøgspersoner ikke opnåede hæmostase på tidspunktet for indgrebet på grund af tidligere ipsilaterale punkturer. Hæmostase blev opnået efter 7 minutter og 37 minutter for disse patienter.

<sup>b</sup> Baseret på en samlet prøvestørrelse på 59: 1 patient blev ikke inkluderet, fordi denne blev lagt i respirator på grund af et lungeødem og ikke kunne mobiliseres i over en uge.

<sup>c</sup> Defineret som en vaskulær komplikation, der kræver blodtransfusion eller operation, eller en lokal infektion, der kræver administration af antibiotika, indlæggelse eller forlængelse af indlæggelse eller debridement af stedet

Der blev ikke observeret større vaskulære komplikationer i Del 1 af forsøget. Der blev rapporteret om 1 større vaskulær komplikation i Del 2 af forsøget: en pseudoaneurisme, som blev rapporteret inden for 1 dag efter proceduren. Hændelsen krævede ultralydsvejledt kompression og en injektion af trombin i pseudoaneurismen og forlængede patientens indlæggelse.

Ud af de 5 uønskede hændelser, der blev rapporteret i Del 1 af forsøget, var der 1 mulig udstyrsrelateret bivirkning: en ikke-alvorlig hændelse med kraftig blødning 1 dag efter indgrebet. Ud af de 19 uønskede hændelser, der blev rapporteret i Del 2 af forsøget, blev der observeret 3 ikke-alvorlige, udstyrsrelaterede, uønskede hændelser med et hæmatom, og der blev observeret 6

mulige, udstyrsrelaterede, ikke-alvorlige, uønskede hændelser, herunder 3 rapporter om vedvarende udsivning, 2 hæmatomer og smerter i 1 ben efter motion.

3 patienter i Del 2 blev betragtet som behandlingssvigt: 2 på grund af manglende opnåelse af hæmostase uden brug af kompression og 1 på grund af den større vaskulære komplikation (pseudoaneurisme). Der var ingen behandlingssvigt i Del 1 af forsøget.

Ud af de seks svigt i forsøgets Del 2 forstyrrede tre ikke proceduren, den ene skyldtes en brugerfejl, den anden var lækage fra indføringshylsteret og én var et knækket filamentled. De to sidste problemer blev håndteret ved hjælp af modelopdateringer implementeret i C11202.

Del 2 af det kliniske forsøg før markedsføring rapporterede ikke de opfølgende resultater efter 6 måneder på grund af manglende patientkomplians. Det kliniske forsøg før markedsføring (EU-SE-001) med 30 dages resultater, som er i overensstemmelse med den kliniske litteraturs opfølgningsperiode, viser, at FemoSeal™ VCS er sikker og effektiv.

#### 1.4.2 Resumé af data fra kliniske forsøg efter markedsføring

Der er udført 4 kliniske forsøg efter markedsføring, som er beskrevet i **tabel 1.6** nedenfor. Disse kliniske undersøgelser er ikke publiceret eller tilgængelige online.

**Tabel 1.6 Gennemførte kliniske forsøg efter markedsføring**

| Gennemførte kliniske forsøg efter markedsføring                                             |              |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                |
|---------------------------------------------------------------------------------------------|--------------|----------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Forsøgets navn                                                                              | År / CI      | Forsøgstype                                              | Formål                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Delmål                                                                                                                                                                                                                                                                                                                     | Potentielle godkendelseskriterier                                                                                                                              |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI | Forsøg efter markedsføring, brugeraccept af ny emballage | Forsøg efter markedsføring udført på modelopdateringen FemoSeal Vascular® Closure System #11202, som har et ændret applikationssystem sammenlignet med den første model, #11200, med henblik på at dokumentere funktionalitet.<br><br>Formålet med forsøget var at få feedback på de reviderede brugsanvisninger (IFU), uddannelsesprojektet for læger og sygeplejersker, at bekræfte de vurderinger, der blev foretaget i risikoanalysen, og at give input til eventuelle forbedringer af produktkvaliteten. | 100 patienter <ul style="list-style-type: none"> <li>63 mænd/37 kvinder</li> <li>Gennemsnitsalder 68 år for kvinder, 65 år for mænd</li> </ul> 2 svenske hospitaler, 6 læger<br><br>112 enheder<br><br>Data indsamlet fra patientjournaler (CRF)<br><br>Planlagt observationstid – 30 minutter fra applikationstidspunktet | Resultater<br><br>1. Illustrationer/instruktioner i brugsanvisningen anses for at være informative og tilstrækkelige<br><br>2. Øjeblikkelig hæmostase (91/100) |

|                                                                                   |                                                         |                                           |                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                  |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-----------------------------------------------------------------------------------|---------------------------------------------------------|-------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|-----|----------|-------|----------|-----------|----|----------|-----------|-------------------------|----------|--------------------|------------|---------------------|-----------|-------------------|---------|-----------------------|----------|--------------------------------|----------|----------------------|-----------|--------------------------|-----------|-----------------------------------|----------|----------------------|--------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008) | Dr. Nicolas Moes<br>Innsbruk Medical University, Østrig | Bekræftende vurdering efter markedsføring | Formålet med dette forsøg var at vurdere sikkerheden ved og ydeevnen af FemoSeal® anvendt under normal klinisk procedure hos patienter, der gennemgik en diagnostisk hjertekateterisering eller en perkutan hjerteinterventionsprocedure udført med 7F-indføringshylster.                                 | 50 fortløbende patienter<br><br>Indikation – diagnostisk eller invasiv hjertekateterisering fra femoralarterien<br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yr)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                                                                                                                                                                                | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yr) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Primære endepunkter <ul style="list-style-type: none"><li>Primært effektendepunkt – TTH (tid til hæmostase) med eller uden udsivning, men uden yderligere kompression, manuel eller mekanisk.</li><li>Sikkerhedsendepunkt – incidens af uønskede hændelser – mindre og større vaskulære komplikationer og alle andre uønskede hændelser – alvorlige og ikke-alvorlige under forsøget (dvs. indtil patienten udskrives).</li></ul> Resultater <ul style="list-style-type: none"><li>Gennemsnitlig tid til hæmostase</li><li>Diagnostik – 56,6 ± 29 sekunder</li><li>Intervention 59,9 ± 16,2 sekunder</li><li>Alle patienter 57,8 ± 26,3</li><li>Alle patienter kunne uden problemer mobiliseres efter 4 timers sengeleje.</li></ul> Sikkerhedsresultater <ul style="list-style-type: none"><li>49/50 (98 %) fri for vaskulære komplikationer indtil udskrivning fra hospitalet</li><li>Gennemsnitlig tid til udskrivning 2,6 dage</li><li>1/50 (2 %) mindre blødning næste dag efter ujævn gang på dagen for angiografi</li></ul> |
| n                                                                                 | 50                                                      |                                           |                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                  |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| men                                                                               | 35 (70%)                                                |                                           |                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                  |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| women                                                                             | 15 (30%)                                                |                                           |                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                  |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| PCI cases                                                                         | 15                                                      |                                           |                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                  |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| age (yr)                                                                          | 62.8±11.1                                               |                                           |                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                  |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| body mass index (kg/m²)                                                           | 25.4±6.7                                                |                                           |                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                  |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| systolic BP (mmHg)                                                                | 131.2±20.9                                              |                                           |                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                  |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| diastolic BP (mmHg)                                                               | 77.9±10.6                                               |                                           |                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                  |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| diabetes mellitus                                                                 | 9 (18%)                                                 |                                           |                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                  |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| arterial hypertension                                                             | 34 (68%)                                                |                                           |                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                  |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| previous coronary intervention                                                    | 13 (26%)                                                |                                           |                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                  |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| preprocedure aspirin                                                              | 50 (100%)                                               |                                           |                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                  |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| preprocedure clopidogrel                                                          | 50 (100%)                                               |                                           |                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                  |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Procedural unfractionated heparin                                                 | 15 (30%)                                                |                                           |                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                  |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Procedural abciximab                                                              | 2 (4%)                                                  |                                           |                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                  |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)    | 2009<br>RADI                                            | Forsøg efter markedsføring                | Forsøget skal informere om, hvorvidt kunderne/brugerne har oplevet problemer med den nye emballage, især den ikke-sterile udvendige side af Tuvek/PET-PE-posen.<br><br>Forsøget skal også give oplysninger om, hvorvidt den behandelende læge opfatter forskelle i udstyrets applikations-/placeringstrin | 25 enheder<br>4 svenske hospitaler<br><br>16/25 (64 %) af patienterne var PCI-patienter med kraftige antikoagulantia                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Resultater<br>1. Emballagerelaterede problemer – 21/25 (84 %) applikationer var vellykkede; 4/25 (16 %) mislykkedes (1– test af ny introducer, 1 indvendig skive gennemtrængte arteriotomi ved det bagerste trin, knap kom op, og den udvendige låseskive blev anbragt i incisionsvævskanalen, 2 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |

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|----------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|---------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                        |                                        |                                                                           | <p>sammenlignet med tidligere anvendte anordninger.</p> <p>Undersøgelsen bør også give input til eventuelle yderligere behov for forbedring af produktkvaliteten.</p>                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | <p>umiddelbar hæmostase blev ikke opnået på trods af ingen problemer ved anlægning).</p> <p>2. Øjeblikkelig hæmostase 19/25 (76 %) patienter</p> <p>3. Blødning 11/25 (44 %) – 9/25 (36 %) sivende/blødende, 2/25 (8 %) hæmatomer</p> <p>Samlet hændelsesrate 19 %</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| <p>The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022)</p> | <p>2022/Terumo Medical Corporation</p> | <p>Et prospektivt, multicenter-observationsforsøg efter markedsføring</p> | <p>Med henblik på yderligere at påvise sikkerheden og effektiviteten af FemoSeal™ VCS med hensyn til at opnå hæmostase gennem adgang via femoralartieren (CFA) hos virkelige forsøgsparticipanter, der gennemgår perkutane endovaskulære procedurer</p> | <ul style="list-style-type: none"> <li>• Patientopfølgning efter 30 dage (<math>\pm</math> 7 dage) ved hospitalsbesøg eller telefonopkald.</li> <li>• Inklusion: december 2021 til juli 2022.</li> <li>• 230 inkluderede forsøgsparticipanter, der gennemgår diagnostiske eller interventionelle endovaskulære procedurer, hvor FemoSeal™ anvendes.</li> </ul> <p>3 europæiske forsøgcentre: Frankrig (92 patienter), Tyskland (38 patienter), Belgien (100 patienter).</p> | <ul style="list-style-type: none"> <li>• <b>Demografi/komorbiditeter:</b> <ul style="list-style-type: none"> <li>- Køn: 161 mænd (70 %)/69 kvinder (30 %).</li> <li>- Gennemsnitsalder: 70 <math>\pm</math> 12.</li> <li>- BMI: 26,1 <math>\pm</math> 4,95 kg/m<sup>2</sup>.</li> <li>- Hypertension: 160 patienter (69,6 %).</li> <li>- Dyslipidæmi: 128 (55,7 %).</li> <li>- Koronararteriesygdom: 42 (18,3 %).</li> <li>- Nuværende ryger: 86 (37,6 %).</li> <li>- Tidligere ryger: 66 (28,8 %).</li> <li>- Koronar hjertesygdom: 34 (14 %).</li> <li>- Tidligere myokardieinfarkt 18 (7,8 %).</li> <li>- Revaskularisering af perifer arterie: 12 (5,2 %) arteria carotis og 83 (37,5 %) arterie i benet.</li> <li>- Antitrombocytbehandling (ved baseline): 211 (91,7 %), herunder 21 (9,1 %) med dobbelt antitrombocytbehandling (DAPT).</li> <li>- Oral antikoagulation: 40 (17,4 %) af patienterne.</li> </ul> </li> <li>• <b>Interventionskarakteristika:</b> <ul style="list-style-type: none"> <li>- Regi: indlagt 162 tilfælde (70,4 %), ambulant 68 tilfælde (29,6 %).</li> </ul> </li> </ul> |

|  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  | <ul style="list-style-type: none"> <li>- Dominerende indikation: claudicatio 147 tilfælde (63,9 %).</li> <li>- Fremgangsmåde: 35 antegrad (15,3 %), 194 retrograd (84,7 %).</li> <li>• <b>Primære endepunkter:</b> <ul style="list-style-type: none"> <li>- Kombineret endepunkt for sikkerhed (frihed for større komplikationer på adgangsstedets ekstremitet inden for 6 timer efter proceduren) og effektivitet (vellykket hæmostase på punkturstedet) opnået hos 215/226 (95,1 %) [95 % CI: 91,46; 97,55] patienter i det komplette analysesæt og 215/230 (93,5 %) [95 % CI 89,47, 96,30] i analysesættet behandlet med FemoSeal™.</li> <li>- Effektivitetsendepunktet blev opnået hos 219/226 (96,9 %) CI [93,7, 98,7] patienter.</li> <li>- Sikkerhedsendepunkt opnået hos 220/230 (95,2 %) [95 % CI: 92,15, 97,90] patienter.</li> </ul> </li> <li>• <b>Sekundære endepunkter:</b> <ul style="list-style-type: none"> <li>- Frihed for mindre komplikationer på adgangsstedet i seks timer efter proceduren opnået hos 225/230 (97,8 %) [95 % CI: 95,00; 99,29].</li> <li>- Frihed for større og mindre komplikationer ved adgangsstedet fra seks timer til 30 dage efter proceduren blev opnået hos 219/230 (95,2 %) [95 % CI: 91,60; 97,59] patienter.</li> <li>- Mediantid til hæmostase med FemoSeal™ VCD:</li> </ul> </li> </ul> |
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|  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|--|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | 0,42 (0,25; 0,50) minutter.<br>- Mediantid til patienten var mobil: 5,00 (4,54; 5,50) minutter.<br>- Medianvarighed af hospitalsophold: 23,98 (22,72, 25,00) timer.<br>- FemoSeal™ VCS' anvendelighed: 'nem' eller 'meget nem' at anlægge hos 98,7 % af tilfældene ('nem' at anlægge hos 21 (9,2 %), 'meget nem' at anlægge hos 205 (89,5 %)) med ingen eller lav modstand ved anlæggelse hos 226 (98,3 %) tilfælde.<br><br>152/230 (66,1 %) af de patienter, der blev behandlet med en guidewire, der var inkluderet i FemoSeal™-sættet (GW 0,038") og anbefalet i FemoSeal™, var uden nogen rapporterede produktmangler eller uønskede hændelser. |
|--|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

2006-forsøget blev udført for at bekræfte sikkerheden og effektiviteten af det aktuelle udstyr med et forbedret applikationssystem og for at få feedback på FemoSeal™ VCS-brugsanvisning og -uddannelsesprogram. Forsøget omfattede 100 patienter, og det primære endepunkt var, om der blev opnået hæmostase, eller om der var behov for yderligere manuelle eller mekaniske kompressioner. Forsøget konkluderede, at anvendelsen af FemoSeal™ VCS var vellykket i flertallet af tilfældene (91 % opnåede øjeblikkelig hæmostase).

2008-forsøget inkluderede 50 patienter for at vurdere sikkerheden og ydeevnen af FemoSeal™ VCS ved brug af normal klinisk praksis hos patienter, der fik foretaget hjertekateterisering med et 7 F-indføringssheath. Det primære endepunkt for forsøget var at indsamle data om tiden til hæmostase og tiden til, at patienten var mobil uden yderligere kompression, manuelt eller mekanisk. Studiets resultater konkluderede, at middeltiden til hæmostase var 57,8 sekunder, og at alle patienter var mobile efter 4 timers sengeleje.

2009-forsøget skulle evaluere den nye FemoSeal™ VCS-emballage. 25 patienter blev inkluderet i forsøget. Det primære endepunkt var, om brugeren havde problemer med emballagen. Brugerne bemærkede ingen problemer med den nye FemoSeal™ VCS-emballage. Dette forsøg indsamlede også data for tiden til hæmostase.

2022-forsøget skulle proaktivt indsamle data om sikkerheden og effektiviteten af FemoSeal VCS med hensyn til at opnå hæmostase gennem adgang via femoralartieren (CFA) hos virkelige forsøgsdeltagere, der gennemgår perkutane endovaskulære procedurer. 230 patienter blev inkluderet i forsøget. De primære endepunkter for registeret er et vellykket forløb (dvs. vellykket hæmostase på punkturstedet) og færre alvorlige komplikationer (f.eks. vaskulær skade, blødning relateret til adgangsstedet, infektion på adgangsstedet, gentagen manuel kompression og ny ipsilateral akut beniskæmi, der er relateret til adgangsstedet). Forsøget konkluderede, at FemoSeal™ VCS fungerer godt i virkelige omgivelser og giver effektiv hæmostase og lave forekomster af komplikationer ved adgangsstedet for patienter, der gennemgår perifere endovaskulære indgreb. Det udviser god ydeevne med kort tid til hæmostase og god feedback fra operatøren om brugervenlighed, hvilket gør FemoSeal™ VCS til en værdifuld anordning til lukning af femoral adgang.

### 1.4.3 Resumé af data fra kliniske forsøg efter markedsføring

#### 1.4.3.1 Gennemført klinisk opfølgning efter markedsføring

Et resumé af de gennemførte kliniske opfølgningsaktiviteter efter markedsføring er beskrevet i **tabel 1.7** nedenfor.

**Tabel 1.7. Kliniske opfølgningsaktiviteter efter markedsføring**

| Gennemførte kliniske opfølgningsaktiviteter efter markedsføring               |                           |                                                                         |                                                                                                                                                                |                                                                                                                                                      |                                                                                                                                                                                                                                                                                                |
|-------------------------------------------------------------------------------|---------------------------|-------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Navn på aktivitet                                                             | År/Virksomhedsoplysninger | Forsøgs-type                                                            | Formål                                                                                                                                                         | Delmål                                                                                                                                               | Potentielle godkendelseskriterier                                                                                                                                                                                                                                                              |
| 2021029<br>2 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021<br>TMC               | Klinisk undersøgelse efter markedsføring – undersøgelse af høj kvalitet | Undersøgelser efter markedsføring for at indsamle prospektiv feedback relateret til brugen af FemoSeal™ Vascular Closure System distribueret på EU-markederne. | <ul style="list-style-type: none"> <li>120 patienter</li> <li>8 enkeltstående læger med &gt; 5 års erfaring</li> <li>Flere lande i Europa</li> </ul> | <b>Evalueringer af enheder på skalaen 1-5 – undersøgelsesudsigten</b> <ul style="list-style-type: none"> <li>Acceptkriterier <ul style="list-style-type: none"> <li>Vurderingerne 3-5 anses for at være gunstige</li> <li>Alle udsagn skal have ≥ 80 % positiv feedback</li> </ul> </li> </ul> |

| Gennemførte kliniske opfølgningsaktiviteter efter markedsføring     |          |                                                                         |                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|---------------------------------------------------------------------|----------|-------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                     |          |                                                                         |                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                              | <ul style="list-style-type: none"> <li>Resultater <ul style="list-style-type: none"> <li>Ingen udsagn i interviewene fik &gt; 20 % ugunstige svar</li> <li>Der blev ikke udfyldt nogen reklamationer over produktet</li> </ul> </li> </ul>                                                                                                                                                                                                                                                        |
| 20210298 – 0.035” and 0038” Guidewire Clinical Survey Report (2021) | 2021 TMC | Klinisk undersøgelse efter markedsføring – undersøgelse af høj kvalitet | Undersøgelse efter markedsføring for at indsamle prospektiv feedback relateret til brugen af den 0,035” guidewire, der følger med 6 Fr Angio-Seal™ VIP Vascular Closure Device (VCD), og den 0,038” guidewire, der følger med både 8 Fr Angio-Seal™ VIP VCD og FemoSeal Vascular Closure System distribueret på EU-markederne. | <ul style="list-style-type: none"> <li>Undersøgelser for 0,035” wire <ul style="list-style-type: none"> <li>106 undersøgelser</li> <li>64 læger</li> </ul> </li> <li>Undersøgelser for 0,038” wire <ul style="list-style-type: none"> <li>109 undersøgelser</li> <li>55 læger</li> </ul> </li> <li>12 retrospektive undersøgelser</li> </ul> | <b>Evalueringer af enheder på skalaen 1-5 – undersøgelsesudsagn</b> <ul style="list-style-type: none"> <li>Acceptkriterier <ul style="list-style-type: none"> <li>Vurderingerne 3-5 anses for at være gunstige</li> <li>Alle udsagn skal have <math>\geq</math> 80 % positiv feedback</li> </ul> </li> <li>Resultater <ul style="list-style-type: none"> <li>Alle guidewirer fik acceptable bedømmelser</li> <li>Der blev ikke indgivet nogen reklamationer over produktet</li> </ul> </li> </ul> |

| Gennemførte kliniske opfølgningsaktiviteter efter markedsføring                                                                       |                     |                                                                         |                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|---------------------------------------------------------------------------------------------------------------------------------------|---------------------|-------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| FemoSeal™<br>Vascular Closure System<br>PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024<br>TMC/TE | Klinisk undersøgelse efter markedsføring – undersøgelse af høj kvalitet | Med henblik på prospektivt at indsamle feedback relateret til brugen af FemoSeal VCS med guidewirer distribueret på EU-markedet. | <ul style="list-style-type: none"> <li>126 undersøgelser               <ul style="list-style-type: none"> <li>7 steder</li> <li>5 lande</li> </ul> </li> <li>14. november 2023 til 11. juni 2024</li> <li>Lægens speciale:               <ul style="list-style-type: none"> <li>Karkirurgi</li> <li>Interventions radiologi</li> <li>Angiologi</li> </ul> </li> </ul> | <b>Evalueringer af enheder på skalaen 5 – undersøgelsesudsagn</b> <ul style="list-style-type: none"> <li>Acceptkriterier               <ul style="list-style-type: none"> <li>Vurderingerne 3-5 anses for at være gunstige</li> <li>Alle udsagn skal have <math>\geq 80\%</math> positiv feedback</li> <li>Hvis der opstår uønskede hændelser i denne undersøgelse, skal de være dem, som risikostyringen forventer.</li> </ul> </li> <li>Patientdemografi               <ul style="list-style-type: none"> <li>Kvinde: 29,4 % (37/126)</li> <li>Mand: 69,8 % (88/126)</li> <li>Køn ikke oplyst: 0,8 (1/126)</li> <li>Alder &gt;75 år: 31,7 %</li> </ul> </li> <li>Resultater               <ul style="list-style-type: none"> <li>Guidewire leveret med FemoSeal™</li> </ul> </li> </ul> |

| Gennemførte kliniske opfølgningsaktiviteter efter markedsføring |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-----------------------------------------------------------------|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                 |  |  |  |  | <p>VCS:<br/>101/126<br/>(80,2 %).</p> <ul style="list-style-type: none"> <li>○ Proceduretid (minutter): 63,4 (36,6) (gennemsnit (SD)); 57,0 (36,0-81,0) (median (IQR))</li> <li>○ Alle vurderinger af FemoSeal™ VCS' ydeevne var gunstige.</li> <li>○ Alle vurderinger af FemoSeal™ VCS-leverede guidewires var gunstige.</li> <li>○ En (0,8 %) uønsket hændelse: FemoSeal™ VCS-skiverne var ikke korrekt justeret, sandsynligvis på grund af brugen af en stiv guidewire (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 tommer), der krævede manuel kompression</li> </ul> |

| Gennemførte kliniske opfølgningsaktiviteter efter markedsføring |  |  |  |  |                        |
|-----------------------------------------------------------------|--|--|--|--|------------------------|
|                                                                 |  |  |  |  | for at opnå hæmostase. |

Terumo Medical Corporation har gennemført tre kvalitetsundersøgelser hos læger i løbet af den aktuelle rapporteringsperiode (01. september 2019 til 31. august 2024).

FemoSeal™ kliniske undersøgelser indsamlede proaktive kliniske data i forhold til sikkerheden og ydeevnen af FemoSeal™ VCS i forbindelse med klinisk brug. Undersøgelsen omfattede spørgsmål, der fokuserede på det samlede udstyr og tilhørende tilbehør, herunder guidewiren på 0,038", og deres direkte interaktioner. De kliniske undersøgelser af guidewiren indsamlede proaktive kliniske data vedrørende sikkerhed og ydeevne i forbindelse med klinisk brug af den 0,038" guidewire, der blev leveret med FemoSeal™ VCS. Spørgsmålene i undersøgelsen fokuserede specifikt på den generelle brug af guidewiren, lige fra indføring gennem indføringsheathet og ind i vaskulaturen til fjernelse af guidewiren.

FemoSeal™ VCS og den 0,038" guidewire, som fulgte med anordningen, fik alle acceptable bedømmelser. Der blev indgivet seks (6) klager over anordningen og ni (9) klager over guidewiren baseret på evaluering af kommentarerne fra de kliniske undersøgelser af høj kvalitet. Klagerne er blevet evalueret for både FemoSeal og guidewiren og blev vurderet som en del af Terumos overvågningsproces efter markedsføring. Der blev ikke identificeret nogen nye risici eller risikoniveauer.

Der blev gennemført en brugerundersøgelse hos læger i 2024 som en del af PMCF-aktiviteterne. Resultaterne af undersøgelsen viste, at FemoSeal™ VCS' ydeevne og sikkerhed generelt var meget gunstige. Kompatibiliteten af andre guidewirer end den standard, der leveres med FemoSeal™ VCS, blev også påvist.

### 1.4.3.2 Igangværende/planlagt klinisk opfølgning efter markedsføring

TMC har én igangværende/planlagt klinisk opfølgningsaktivitet efter markedsføring. Der vil blive gennemført en klinisk spørgeundersøgelse med henblik på prospektivt at indsamle feedback relateret til brugen af guidewiren med FemoSeal VCS distribueret på EU-markedet. Spørgeskemaet udfyldes af læger med henblik på at undersøge, hvilke guidewirer de brugte under proceduren. Formålet med denne undersøgelse er at adressere et hul, der er identificeret som mangel på litteratur og kommentarer fra eksterne reviewere om FemoSeal™ VCS' kompatibilitet med brugen af andre guidewirer fra ikke-Terumo-mærker. Feedback omfatter tekniske resultater, klinisk ydeevne og sikkerhed i forbindelse med anordningens ydeevne med forskellige guidewirer.

#### 1.4.4 Sammenfatning af data fra systematisk litteraturgennemgang

Terumo Medical Corporation gennemfører systematiske litteraturgennemgange for at indsamle og evaluere kliniske sikkerheds- og ydeevnedata fra offentliggjorte forsøg med FemoSeal™ VCS og/eller lignende udstyr. Formålet med den årlige screening af den offentliggjorte litteratur er at identificere tidligere ukendte bivirkninger, overvåge kendte bivirkninger, identificere nye risici og identificere muligt systematisk misbrug eller off-label brug af FemoSeal™ VCS.

Den seneste systematiske litteraturgennemgang, som omfattede perioden fra 1. september 2019 til og med 31. august 2024, identificerede 29 offentliggjorte forsøg, som gav kliniske sikkerheds- og ydeevnedata om FemoSeal™ VCS. Der var 23 referencer, der rapporterede om on-label brug af FemoSeal™ VCS, og off-label brug blev rapporteret i ni studier. Samlet set viser litteraturgennemgangen af forsøg, der specifikt omhandler brugen af FemoSeal™ VCS, en forsøgspopulation, som er repræsentativ for patienter i EU, der gennemgår perkutane vaskulære kateteriseringsprocedurer. Se **afsnit 3** for en liste over disse 23 on-label, fagfællebedømte publikationer.

Den kliniske ydeevne blev vurderet ved hjælp af følgende målinger:

- Tiden til hæmostase er bedre end eller sammenlignelig med den nyeste teknologi for almindelig perkutan lukning af femoralarterien.
- Tiden til mobilisering er bedre end eller sammenlignelig med den nyeste teknologi til perkutan lukning af femoralarterien.
- Hyppigheden af postoperative komplikationer er sammenlignelig eller lavere end den aktuelle behandlingsstandard.

På baggrund af disse kliniske præstationsmål viste dataene i denne litteraturgennemgang, at FemoSeal™ VCS med succes kan anvendes til at lukke punktur af femoralarterien (arteriotomi) hos patienter, som har fået foretaget perkutan kateterisation ved hjælp af et 7 Fr eller mindre indføringshylster. Komplet hæmostase blev opnået hos størstedelen af patienterne (79,65-100 %) og var forbundet med en mediantid til hæmostase på 0,5 min., gennemsnitlig tid til udskrivelse var 3 dage. Mellem 69,2-86,7 % af patienterne var i stand til at gå 5 timer efter lukning med en gennemsnitlig postoperativ sengeleje på 349 min. Der blev observeret svigt af FemoSeal™ VCS i 3,68-4 % af tilfældene, og yderligere manuel kompression var nødvendig i 0,9-4,4 % af procedurerne.

Klinisk sikkerhed blev vurderet ved uønskede hændelser, herunder, men ikke begrænset til:

- Blødning
- Hæmatom
- Pseudoaneurisme
- Blå mærker

- Arteriovenøs fistel
- Infektion
- Død

For hver af disse uønskede hændelser var den rapporterede incidensrate for FemoSeal™ VCS i de inkluderede studier mindre end eller svarende til tidligere rapporterede forekomster for manuelle kompressionsanordninger og andre vaskulære lukkeanordninger.

Der blev ikke identificeret nogen uønskede hændelser ved gennemgang af 10 case-rapporter, da der ikke blev identificeret nogen nye, uventede, opståede eller uacceptable risici.

Den overordnede effektivitet ved brug af FemoSeal™ VCS under diagnostisk angiografi eller interventionelle operationer afhænger af flere faktorer som f.eks. køn, alder, patientens anatomi, komorbiditeter, anatomisk placering af punkturstedet, kirurgens erfaring, VCD-anlæggelsesmetode, postoperativ pleje, osv. Ud over teknisk succes, herunder opnåelse af hæmostase, gav FemoSeal™ VCS kliniske fordele i forhold til vaskulær lukning efter punktering af femoralarterien, såsom reduktion af tiden til hæmostase og reduktion af tiden til mobilisering. Ydeevneresultaterne for FemoSeal™ VCS er i overensstemmelse med dem, der forventes for denne type anordning, når den anvendes som tilsigtet. Nogle af de referencer, der blev indhentet i løbet af den aktuelle søgeperiode, viste anvendelse af forsøgsproduktet på et andet anatomisk sted end femoralarterien og til lukning af arteriotomier > 7 Fr, hvilket betragtes som off-label.

Der blev ikke identificeret ukendte bivirkninger, nye risici eller mulig systematisk misbrug af anordningen under gennemgangen. Hvis FemoSeal™ VCS imidlertid anvendes med forsigtighed af uddannede læger, fungerer det medicinske udstyr som et nyttigt og nødvendigt klinisk udstyr. Samlet set imødekommer målbehandlingen og dermed FemoSeal™ VCS det kliniske behov, der i øjeblikket eksisterer ved behandling af komplikationer relateret til vaskulær adgang.

Samlet set viste dataene i denne litteraturgennemgang ingen præstations- eller sikkerhedsmæssige problemer i forbindelse med kliniske forsøg, som ikke tidligere var kendt, eller negative effekter, som forekom med højere hyppighed end forudset/acceptabelt. Det kan derfor ud fra denne litteraturgennemgang konkluderes, at FemoSeal™ VCS, når systemet anvendes til at give kompression med henblik på hæmostase ved arteriotomien efter perkutan kateterisering, fortsat fungerer som forventet og ikke er forbundet med alvorlige sikkerhedshændelser.

#### **1.4.5 Resumé af data fra overvågning efter markedsføring**

Et proaktivt PMS-system er på plads, og en gennemgang af alle klager gennemføres månedligt og i overensstemmelse med interne produktionsprocedurer. Reklamationsdata blev analyseret i perioden 1. september 2019 til 31. august 2024. Overordnet set var der 28 indberetninger om overvågning af medicinsk udstyr (MDV) og 476 indberetninger om kundereklamationer til producenten. Af de 28 MDV-rapporter var 27 relateret til uønskede hændelser og en til funktionsfejl i anordningen. Der var to dødsfald i rapporteringsperioden, men ingen af de rapporterede dødsfald blev vurderet at være relateret til forsøgsproduktet. Blandt de 476



reklamationer, der blev indgivet til producenten, var de hyppigste årsager til reklamationerne vanskeligheder ved anlæggelse (146 tilfælde, 0,0142 % forekomsthypighed). Fejltilstand for udtrækningshændelser er den næstmest almindelige med en frekvens på 0,0126 % (130 hændelser).

FemoSeal Vascular Closure System har over 1.030.136 salg globalt og 827.843 i Det Europæiske Økonomiske Samarbejdsområde. Den beregnede reklamationshypighed baseret på globalt salg er 0,046 %. Den samlede procent af kundeklager er meget lav. Der blev ikke identificeret nye risici, som ikke er inkluderet i brugsanvisningen og risikodokumentationen.

Incidensrater for bivirkninger er vist i **tabel 1.2**. Der blev ikke identificeret nogen nye uventede, opståede eller uacceptable risici i forbindelse med reklamationerne. Der var ingen signifikante stigninger i hypigheden eller sværhedsgraden af kendte bivirkninger.

#### 1.4.6 Samlet resumé af klinisk ydeevne og sikkerhed

FemoSeal™ VCS er indiceret til brug ved lukning af punkturen af femoralarterien (arteriotomi) hos patienter, som har fået foretaget perkutan kateterisation ved hjælp af et 7F (2,33 mm) eller mindre indføringshylster. Denne kliniske evaluering er baseret på en omfattende analyse af tilgængelige kliniske data og litteratur før og efter markedsføring, der er relevante for den tilsigtede brug af FemoSeal™ VCS.

Der er foretaget en omfattende gennemgang af den offentliggjorte litteratur i perioden fra 1. september 2019 til og med 31. august 2024. Evidensen omfattede 29 forsøg med FemoSeal™ VCS. Den evidens, der er fremlagt i den kliniske evaluering, konkluderer, at forsøgsproduktet, når det anvendes som indiceret, er sikkert og effektivt, og at eventuelle risici eller uønskede bivirkninger, der kan være forbundet med produktet under normale brugsforhold, udgør acceptable risici og opvejes af fordelene for patienten. Ydeevneresultaterne for forsøgspersonernes anordninger er i overensstemmelse med dem, der forventes for denne type anordning, når den anvendes som tilsigtet.

De potentielle bivirkninger, der er forbundet med brugen af FemoSeal™ VCS, omfatter de bivirkninger, der almindeligvis rapporteres med alternative metoder til lukning af arteriotomi, f.eks. blødning og hæmatom. Samlet set svarer incidensraten for de bivirkninger, der er indberettet ved brug af FemoSeal™ VCS, til dem, der er indberettet ved manuel kompression og lignende vaskulære lukkeanordninger. Specifikt for blødning og hæmatom er den rapporterede hypighed for FemoSeal™ VCS mindre end den rapporterede hypighed for lignende vaskulære lukkeanordninger. Hver enkelt af de rapporterede uønskede hændelser, både fra den offentliggjorte litteratur og fra overvågningen efter markedsføringen, var tidligere blevet identificeret (se **afsnit 1.3**).

De eksisterende data vedrørende den kliniske sikkerhed og ydeevne for FemoSeal VCS tyder på, at patientfordelene ved brug af denne vaskulære lukkeanordning opvejer mulige risici, når den anvendes i overensstemmelse med brugsanvisningen.

Som angivet i de foregående afsnit ovenfor viser dataene for FemoSeal™ VCS overensstemmelsen mellem de data, der er relateret til den enhed, der evalueres (f.eks. brug af udstyret, sikkerhedsudfald, klinisk ydeevne og kliniske fordele), identificerede ækvivalente anordninger og de data, der er relateret til lignende anordninger, der er anført med den nyeste teknologi.

Krydsanalysen af sikkerhedsdata identificerede ingen huller mellem følgende:

- Data, der er omtalt i den nyeste teknologi
- Data, der er specifikke for det udstyr, der evalueres
- Data, der er nævnt i risikostyringsfil(er)
- Data, der er nævnt i mærkningen og/eller brugsanvisningen (dvs. resterende risici, der skal overføres til brugeren, behandles).

Den kliniske sikkerhed er blevet påvist ved lave komplikationsrater, der er identificeret i den offentliggjorte fagfællebedømte kliniske litteratur, virksomhedssponsorerede kliniske forsøg, gennemgang af data efter markedsføring sammenkoblet med ingen tilbagetrækninger fra markedet. Der er ikke identificeret nogen fejl med hensyn til funktionen. Den gennemgæede litteratur beskrev anvendelse af FemoSeal™ VCS, som var i overensstemmelse med producentens tilsigtede brug.

## **1.5 Mulige diagnostiske eller terapeutiske alternativer**

Manuel kompression anvendes traditionelt til at opnå hæmostase på arteriotomistedet efter vaskulære kateterisationer. Manuel kompression er blevet forbundet med immobilisering af patienten i længere perioder (op til 8 timer efter en procedure) og med betydeligt ubehag og forlængede hospitalsophold. En nylig systematisk gennemgang viste, at mediantiden til opnåelse af hæmostase med manuel kompression var 20,8 minutter.<sup>1</sup>

Alternativer til manuel kompression omfatter eksterne hæmostatiske anordninger, der påfører mekanisk kompression på arteriotomistedet. Disse anordninger forkorter ikke tiden til hæmostase eller tiden til, at patienten er mobil, men reducerer kravene til personalet ved at erstatte manuel kompression med mekanisk kompression. Hyppigheden af uønskede hændelser i forbindelse med brug af mekanisk kompression svarer til hyppigheden med manuel kompression.

Vaskulære lukkeanordninger, såsom FemoSeal™ VCS, er designet til at lukke arteriotomien. De har til formål at reducere tiden til hæmostase og muliggøre tidligere mobilitet. En nylig systematisk gennemgang af 13 kommercielt tilgængelige anordninger, viste, at mediantiden til opnåelse af hæmostase med en vaskulær lukkeanordning var 5,4 minutter. Mediantiden til

hæmostase for de enkelte vaskulære lukkeanordninger varierede fra 1 minut (FemoSeal™ VCS) til 14 minutter, hvor størstedelen af anordningerne lå mellem 4 og 10 minutter.<sup>1</sup>

Almindeligt rapporterede bivirkninger, der er forbundet med lukning af arteriotomistedet med manuelle kompressioner, eksterne hæmostatiske anordninger eller vaskulære lukkeanordninger omfatter hæmatom, blødning ved adgangsstedet, pseudoaneurisme, arteriovenøs fistel og infektion. Den samme systematiske gennemgang (34 randomiserede kontrollerede forsøg, 14.401 patienter) fandt, at forekomsten af uønskede hændelser var ens mellem manuel kompression og brugen af vaskulære lukkeanordninger, bortset fra at blødning havde en tendens til at være lidt højere med vaskulære lukkeanordninger.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Forslag til brugerprofil og uddannelse

De tilsigtede brugere af FemoSeal™ Vascular Closure System er læger med en uddannelse, der kvalificerer dem til at udføre arteriel adgang og lukning i forbindelse med endovaskulære procedurer gennem femoralarterien, og som har deltaget i et Terumo Medical Corporations FemoSeal™ lægevejledningsprogram.

## 1.7 Relevante harmoniserede og fælles standarder

| Standardreference | Indeværende år for komplians/rev. | Beskrivelse                                                                                                                              |
|-------------------|-----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070         | 2014/AMD1:2018                    | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070      | 2014/A1:2018                      | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance      | 20. maj 2021                      | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052        | 2015                              | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |

| Standardreference | Indeværende<br>år for<br>komplians/rev. | Beskrivelse                                                                                                                                                              |
|-------------------|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F2213        | 2017                                    | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment                                             |
| ASTM F2503        | 2020                                    | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                                                           |
| ASTM F2182        | 2019                                    | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging                                    |
| EN ISO 13485      | 2016/A11:2021                           | Medical devices – Quality management systems – Requirements for regulatory purposes                                                                                      |
| ISO 13485         | 2016                                    | Medical devices – Quality management systems – Requirements for regulatory purposes                                                                                      |
| ISO 14644-1       | 2015                                    | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1    | 2015                                    | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2       | 2015                                    | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2    | 2015                                    | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3       | 2019                                    | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3    | 2019                                    | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |

| Standardreference      | Indeværende<br>år for<br>komplians/rev. | Beskrivelse                                                                                                                                      |
|------------------------|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14698-1            | 2003                                    | Cleanrooms and associated controlled environments<br>— Biocontamination control — Part 1: General principles and methods                         |
| EN ISO 14698-1         | 2003                                    | Cleanrooms and associated controlled environments<br>— Biocontamination control — Part 1: General principles and methods                         |
| ISO 14698-2            | 2003/TC1:2004                           | Cleanrooms and associated controlled environments<br>— Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| EN ISO 14698-2         | 2003/TC 1:2004                          | Cleanrooms and associated controlled environments<br>— Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| USP <788>              | Ikke relevant                           | TEST FOR PARTIKLER I INJEKTIONER                                                                                                                 |
| EU-farmakopé<br>2.9.19 | Ikke relevant                           | Particulate Contamination: Sub-Visible Particles                                                                                                 |
| IEC 62366-1            | 2015                                    | Medical devices — Part 1: Application of usability engineering to medical devices                                                                |
| EN 62366-1             | 2015                                    | Medical devices — Part 1: Application of usability engineering to medical devices                                                                |
| EN ISO 14971           | 2019/A11:2021                           | Medical devices — Application of risk management to Medical devices                                                                              |
| ISO 14971              | 2019                                    | Medical devices — Application of risk management to Medical devices                                                                              |
| ASTM F1980             | 2016                                    | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                                              |
| EN ISO 10993-1         | 2020                                    | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                       |
| ISO 10993-1            | 2018                                    | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                       |

| Standardreference | Indeværende<br>år for<br>komplians/rev. | Beskrivelse                                                                                                                |
|-------------------|-----------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-2    | 2006                                    | Biological evaluation of medical devices — Part 2:<br>Animal welfare requirements                                          |
| ISO 10993-2       | 2006                                    | Biological evaluation of medical devices — Part 2:<br>Animal welfare requirements                                          |
| EN ISO 10993-3    | 2014                                    | Biological evaluation of medical devices – Part 3:<br>Tests for genotoxicity, carcinogenicity and<br>reproductive toxicity |
| ISO 10993-3       | 2014                                    | Biological evaluation of medical devices – Part 3:<br>Tests for genotoxicity, carcinogenicity and<br>reproductive toxicity |
| EN ISO 10993-4    | 2017                                    | Biological Evaluation of Medical Devices- Part 4:<br>Selection of tests for interactions with blood                        |
| ISO 10993-4       | 2017                                    | Biological Evaluation of Medical Devices- Part 4:<br>Selection of tests for interactions with blood                        |
| EN ISO 10993-5    | 2009                                    | Biological evaluation of medical devices – Part 5:<br>Tests for in vitro cytotoxicity                                      |
| ISO 10993-5       | 2009                                    | Biological evaluation of medical devices – Part 5:<br>Tests for in vitro cytotoxicity                                      |
| EN ISO 10993-6    | 2016                                    | Biological evaluation of medical devices - Part 6:<br>Tests for local effects after implantation                           |
| ISO 10993-6       | 2016                                    | Biological evaluation of medical devices - Part 6:<br>Tests for local effects after implantation                           |
| EN ISO 10993-10   | 2023                                    | Biological evaluation of medical devices —Part 10:<br>Tests for irritation and skin sensitization                          |
| ISO 10993-10      | 2021                                    | Biological evaluation of medical devices —Part 10:<br>Tests for irritation and skin sensitization                          |
| EN ISO 10993-11   | 2018                                    | Biological evaluation of medical devices — Part 11:<br>Tests for systemic toxicity                                         |
| ISO 10993-11      | 2017                                    | Biological evaluation of medical devices — Part 11:<br>Tests for systemic toxicity                                         |

| Standardreference | Indeværende år for<br>komplians/rev. | Beskrivelse                                                                                                                                |
|-------------------|--------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-12   | 2021                                 | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| ISO 10993-12      | 2021                                 | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| EN ISO 10993-17   | 2009                                 | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17      | 2002                                 | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18      | 2020/A1:2022                         | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |
| EN ISO 10993-18   | 2020/A1:2022                         | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |
| EN ISO 10993-23   | 2021                                 | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |
| ISO 10993-23      | 2021                                 | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |
| ASTM F2382        | 2018                                 | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)          |
| ASTM F756         | 2017                                 | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                      |
| USP <85>          | Ikke relevant                        | [Bacterial Endotoxins Test. (Sterility)]                                                                                                   |

| Standardreference      | Indeværende<br>år for<br>komplians/rev. | Beskrivelse                                                                                                                                                                  |
|------------------------|-----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| USP <161>              | Ikke relevant                           | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI<br>ST72:2011 | 2019                                    | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135           | 2014/A1:2019                            | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135              | 2014/A1:2018                            | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7         | 2008/A1:2022                            | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |
| ISO 10993-7            | 2008/A1:2019                            | Biological evaluation of medical devices — Part 7: Ethylenoxid                                                                                                               |
| EN 556-1               | 2024                                    | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices              |
| EN ISO 11737-1         | 2018/A1:2021                            | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                                        |
| ISO 11737-1            | 2018/A1:2021                            | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                                        |
| EN ISO 11138-1         | 2017                                    | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                                 |
| ISO 11138-1            | 2017                                    | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                                 |



| Standardreference | Indeværende<br>år for<br>komplians/rev. | Beskrivelse                                                                                                                              |
|-------------------|-----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 11138-2    | 2017                                    | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| ISO 11138-2       | 2017                                    | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| EN ISO 15223-1    | 2016                                    | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| ISO 15223-1       | 2016                                    | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| EN 1041           | 2008/A1:2013                            | Information supplied by the manufacturer of medical devices                                                                              |
| EN ISO 11607-1    | 2020/A1:2023                            | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| ISO 11607-1       | 2019/A1:2023                            | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| EN ISO 11607-2    | 2020/A1:2023                            | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes       |
| ISO 11607-2       | 2019/A1:2023                            | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes       |
| ASTM D4169        | 2016                                    | Standard Practice for Performance Testing of Shipping Containers and Systems                                                             |
| ASTM F1886/F1886M | 2016                                    | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                      |

| Standardreference | Indeværende<br>år for<br>komplians/rev. | Beskrivelse                                                                                                                                                                        |
|-------------------|-----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F2825        | 2018                                    | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                           |
| ASTM F2096        | 2011 (R 2019)                           | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                                       |
| ASTM F88/F88M     | 2015                                    | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                               |
| MDCG 2021-24      | 2021                                    | Guidance on classification of medical devices                                                                                                                                      |
| MDCG 2020-3       | 2020                                    | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD         |
| MDCG 2020-8       | 2020                                    | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                                     |
| MDCG 2020-7       | 2020                                    | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                                  |
| MDCG 2020-6       | 2020                                    | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                               |
| MDCG 2019-9 v1    | 2022                                    | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                           |
| MDCG 2019-8 v2    | 2020                                    | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices |
| MDCG 2020-15      | 2020                                    | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                           |
| MDCG 2021-11      | 2021                                    | Guidance on Implant Card – ‘Device types’                                                                                                                                          |

| Standardreference      | Indeværende<br>år for<br>komplians/rev. | Beskrivelse                                                                                                                                                                                                                                                   |
|------------------------|-----------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2021-19           | 2021                                    | Guidance note integration of the UDI within an organisation's quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4         | 2021                                    | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2            | 2019                                    | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1            | 2019                                    | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7            | 2018                                    | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6            | 2018                                    | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |
| MDCG 2018-4            | 2018                                    | MDCG 2018-4 Annex: UDI database Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                                                                                                  |
| MDCG 2018-3 v1         | 2020                                    | Guidance on UDI for systems and procedure packs                                                                                                                                                                                                               |
| MDCG 2021-25           | 2021                                    | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC                                                                 |
| Meddev 2.12-2<br>Rev 2 | 2012                                    | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                                                                                        |

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### 3.0 REVISIONSHISTORIK

| SSCP-revisionsnummer      | Udgivelsesdato  | Ændringsbeskrivelse                                                  | Revision godkendt af det bemyndigede organ                                                                                                                                                                                                                                                                           |
|---------------------------|-----------------|----------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022              | 20. januar 2023 | Første udgave, ved MDR CE-certificering                              | <input checked="" type="checkbox"/> Ja<br>Valideringssprog: English<br><input type="checkbox"/> Nej (gælder kun for klasse IIa eller visse IIb implanterbare anordninger (MDR, artikel 52, stk. 4, andet afsnit), for hvilke SSCP endnu ikke er valideret af NB)<br><input type="checkbox"/> Andet (uddyb venligst): |
| SSCP-FS-2023 – Revision 1 | 15. marts 2024  | Opdateret for perioden 1. januar 2019 til og med 31. december 2023.  | <input checked="" type="checkbox"/> Ja<br>Valideringssprog: English<br><input type="checkbox"/> Nej (gælder kun for klasse IIa eller visse IIb implanterbare anordninger (MDR, artikel 52, stk. 4, andet afsnit), for hvilke SSCP endnu ikke er valideret af NB)<br><input type="checkbox"/> Andet (uddyb venligst): |
| SSCP-FS-2024 Revision 1   |                 | Opdateret for perioden 1. september 2019 til og med 31. august 2024. | <input type="checkbox"/> Ja<br>Valideringssprog: English<br><input type="checkbox"/> Nej (gælder kun for klasse IIa eller visse IIb implanterbare anordninger (MDR, artikel 52, stk. 4, andet afsnit), for hvilke SSCP endnu ikke er valideret af NB)<br><input type="checkbox"/> Andet (uddyb venligst):            |

|                            |               |                                                            |                                                                                                                                                                                                                                                                                                                                                         |
|----------------------------|---------------|------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>Revision 2 | June 20, 2025 | Revideret på baggrund af NSAI-forespørgsler til validering | <div><input checked="" type="checkbox"/> Ja</div> <div>Valideringssprog: English</div> <div><input type="checkbox"/> Nej (gælder kun for klasse IIa eller visse IIb implanterbare anordninger (MDR, artikel 52, stk. 4, andet afsnit), for hvilke SSCP endnu ikke er valideret af NB)</div> <div><input type="checkbox"/> Andet (uddyb venligst):</div> |
|----------------------------|---------------|------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|



**Kurzbericht über Sicherheit und klinische Leistung**

**FemoSeal™ Vascular Closure System**

|                                                                |                                                                                             |
|----------------------------------------------------------------|---------------------------------------------------------------------------------------------|
| <b>Hersteller</b>                                              | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 USA         |
| <b>Einheitliche Registrierungsnummer des Herstellers (SRN)</b> | US-MF-000019594                                                                             |
| <b>Managementbeauftragte(r)/PRRC</b>                           | Kimberly Feitl<br>Vice President, Quality                                                   |
| <b>Basis UDI-DI</b>                                            | 38970FS79                                                                                   |
| <b>EMDN-Nummer</b>                                             | C900199 – Hämostasesysteme – Sonstige                                                       |
| <b>Produktklasse</b>                                           | Klasse III                                                                                  |
| <b>Jahr der ersten CE-Kennzeichnung des Produkts</b>           | 2005                                                                                        |
| <b>EU-Vertreter</b>                                            | Terumo Europe N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgien<br>SRN: BE-AR-000001433 |
| <b>Benannte Stelle</b>                                         | NSAI<br>CE 0050                                                                             |

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Durch diesen Kurzbericht über die Sicherheit und klinische Leistung (Summary of Safety and Clinical Performance, SSCP) soll die Öffentlichkeit eine aktualisierte Zusammenfassung der wichtigsten Aspekte der Sicherheit und der klinischen Eigenschaften des FemoSeal™ Vascular Closure Systems (VCS) erhalten.

Einen Kurzbericht über Sicherheit und klinische Leistung des Produkts für Anwender/medizinisches Fachpersonal finden Sie in **Abschnitt 1.0**.

## **1.0 KURZBERICHT FÜR ANWENDER/MEDIZINISCHES FACHPERSONAL**

Der SSCP soll die Bedienungsanleitung, die das wichtigste Dokument zur Sicherstellung der gefahrlosen Verwendung des Produkts ist, nicht ersetzen und den Anwendern oder den Patienten auch keine diagnostischen oder therapeutischen Anregungen geben. Der SSCP ersetzt nicht die Pflichtangaben auf den Implantatausweisen oder in anderen Pflichtdokumenten.

### **1.1 Bestimmungsgemäße Verwendung des Produkts**

#### **1.1.1 Bestimmungsgemäße Verwendung**

Das FemoSeal™ Vascular Closure System ist ein Medizinprodukt zum Verschließen einer Arterienpunktion nach perkutaner Katheterisierung durch die A. femoralis communis.

#### **1.1.2 Indikationen**

Das FemoSeal™ Vascular Closure System ist für das Verschließen der A. femoralis communis (Arteriotomie) bei perkutaner Katheterisierung mit einer Prozedurdurchleuse 7F (2,33 mm) oder kleiner indiziert.

#### **1.1.3 Kontraindikationen und/oder Einschränkungen**

Das FemoSeal™ Vascular Closure System ist kontraindiziert bei Patienten mit Arteriotomien, bei denen Schleusen oder Produkte mit einem Durchmesser von mehr als 2,33 mm (7F) verwendet wurden.

#### **1.1.4 Patientenpopulationen**

Die Sicherheit und Wirksamkeit des FemoSeal™ Vascular Closure Systems wurde bei Patienten ab 18 Jahren nachgewiesen, die sich einer perkutanen Katheterisierung mit einer Prozedurdurchleuse 7F (2,33 mm) oder kleiner unterzogen haben.

#### **1.1.5 Besondere Patientenpopulationen**

Die Sicherheit und Wirksamkeit des FemoSeal™ Vascular Closure Systems wurde bei den folgenden Patientengruppen nicht nachgewiesen:

- Patienten mit vorbestehender Autoimmunerkrankung.
- Patienten, die sich einer therapeutischen Thrombolysebehandlung unterziehen.
- Patienten mit klinisch signifikanter peripherer Gefäßerkrankung.
- Patienten mit unkontrollierter Hypertonie (> 220 mmHg systolisch oder > 110 mmHg diastolisch).

- Patienten mit einer Blutungsstörung, einschließlich Thrombozytopenie ( $< 100.000$  Thrombozyten) oder Anämie ( $\text{Hgb} < 10 \text{ mg/dl}$ ).
- Patienten, bei denen das Innenlumen der A. femoralis communis kleiner als 5 mm ist.
- Patienten mit Nieren- und/oder Leberfunktionsstörungen.
- Patienten mit anderen relevanten Komorbiditäten.
- Patienten bestimmter Abstammung und/oder ethnischer Herkunft.
- Patienten, die vor weniger als 72 Stunden einen Myokardinfarkt erlitten haben.
- Patienten mit einem Gefäßersatz oder Stent an der Punktionsstelle.
- Schwangere oder stillende Patientinnen.
- Patienten unter 18 Jahren.

### 1.1.6 Vorgesehene Anwender

Vorgesehene Anwender des FemoSeal™ Vascular Closure Systems sind Ärztinnen und Ärzte mit der erforderlichen Qualifizierung, um arterielle Zugänge und Verschlüsse bei endovaskulären Eingriffen über die A. femoralis communis herstellen zu dürfen, die an einem ärztlichen FemoSeal™ Schulungsprogramm der Terumo Medical Corporation teilgenommen haben.

## 1.2 Produktbeschreibung

### 1.2.1 Beschreibung des Produkts

Das von der Terumo Medical Corporation (TMC) hergestellte FemoSeal™ Vascular Closure System ist ein resorbierbares Gefäßverschlussystem, das entwickelt wurde, um nach einer perkutanen Katheterisierung durch die A. femoralis communis eine femorale arterielle Hämostase zu erreichen.

FemoSeal™ Verschlusselemente bestehen aus zwei resorbierbaren Polymerscheiben, der Innendichtung und der äußeren Sperrscheibe, die durch ein resorbierbares Multifilament zusammengehalten werden und so die Arteriotomie mechanisch abdichten (siehe **Abbildung 1.1** und **Abbildung 1.2**). Nach dem Entfalten durch die Kegelschleuse wird die äußere Sperrscheibe auf die Multifilamentwelle gedrückt, was zu einem mechanischen Verschluss der Punktionsstelle zwischen der Innendichtung und der äußeren Sperrscheibe führt. Die Innendichtung und die äußere Sperrscheibe werden durch Reibung auf der Multifilamentwelle gehalten. Die Hämostase wird mechanisch erzielt. Die Verschlusselemente werden durch Hydrolyse abgebaut.

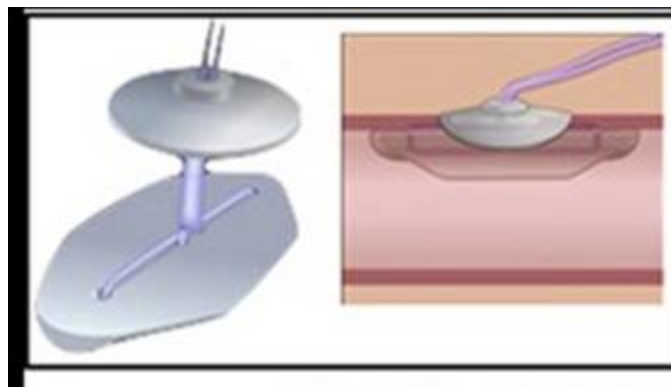
Die implantierbaren Verschlusskomponenten, die Innendichtung und die äußere Sperrscheibe werden innerhalb von achtzehn (18) Monaten abgebaut, während das Multifilament

schätzungsweise nach zwei (2) bis drei (3) Jahren abgebaut und durch Hydrolyse vom umliegenden Gewebe absorbiert wird. In Tests wurde die Fähigkeit der implantierbaren Verschlusskomponenten nachgewiesen, die Kompression auf der Arteriotomie bis zu acht (8) Stunden aufrechtzuerhalten. Die Abbauprodukte werden metabolisiert und im Urin ausgeschieden oder als Kohlendioxid über die Lunge ausgeatmet. In Tierversuchen wurden keine Akkumulationseffekte beobachtet. Die zusätzlichen Komponenten des FemoSeal™ Vascular Closure Systems, die während des Eingriffs mit lebendem Gewebe oder Blut in Kontakt kommen, sind Kegelschleuse, Dilatator, Tamper, Pusher und Führungsdraht.

**Abbildung 1.1 Innendichtung und äußere Sperrscheibe**

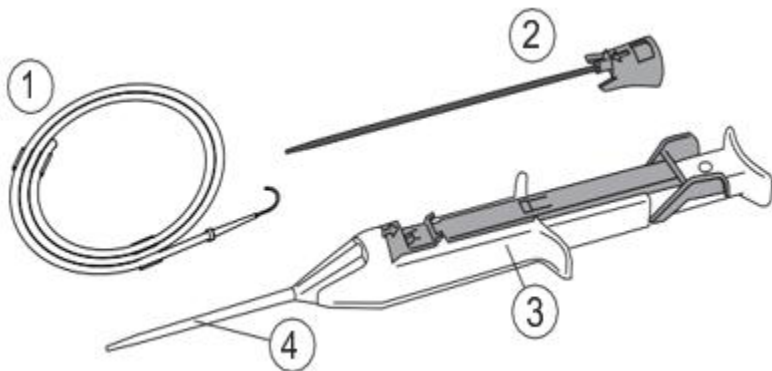


**Abbildung 1.2 Innendichtung und äußere Sperrscheibe eingesetzt**



Die FemoSeal™ Einheit wird zusammen mit einem Dilatator und einem Führungsdraht mit 0,038" (0,97 mm) Außendurchmesser, 27,5" (70 cm) Länge sowie einer J-Spitze geliefert, siehe **Abbildung 1.3** unten. Der Führungsdraht befindet sich in einem Polyethylenschlauch. Alle Teile sind in einer stabilen Papierkassette verpackt. Die Verpackung enthält auch den Implantatausweis für den/die Patienten/Patientin. Das FemoSeal™ Vascular Closure System erfordert kein zusätzliches Zubehör, um wie vorgesehen zu funktionieren. Das Produkt ist nur für die Verwendung mit dem Dilatator und dem Führungsdraht vorgesehen, die in der Produktverpackung enthalten sind.

Abbildung 1.3 FemoSeal™ VCS Einheit mit Führungsdraht und Dilatator



### 1.2.2 Materialien und Komponenten

In **Tabelle 1.1** unten sind die Komponenten des FemoSeal™ VCS aufgeführt.

**Tabelle 1.1 FemoSeal™ VCS Materialien und Komponenten**

| Teilenummer | Beschreibung                                      |                                                       | Materialien                                                                                                                                                                                           |
|-------------|---------------------------------------------------|-------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1           | Führungsdraht 0,038" (0,97 mm) mit einer J-Spitze |                                                       | Führungsdraht: Edelstahl 304<br><br>J-Spitze: Polypropylen, Violett pigment<br><br>Clip: Polyethylen<br><br>Schläuche: Polyethylen                                                                    |
| 2           | FemoSeal Dilatator                                |                                                       | Ansatz: Tetrahydrofuran, Blaupigment, Polybutylenterephthalat (PBT)<br><br>Schlauch: Hochdichtes Polyethylen (HDPE), Schwarzpigment<br><br>Gleitmittel: Silikon Dow Corning 360                       |
| 3/4         | FemoSeal Einheit                                  | RD7, geformt – Innendichtung und äußere Sperrscheibe* | Copolymer aus Glykolid, Trimethylencarbonat, ε-Caprolacton und TMP: Trimethylolpropan (Initiator)                                                                                                     |
|             |                                                   | Multifilament*                                        | Segmentiertes Copolymer aus L,L-Lactid, Trimethylencarbonat, ε-Caprolacton und 1,3-Propandiol (Initiator)<br><br>Die Beschichtung besteht aus einem Copolymer aus Glykolid, ε-Caprolacton und L-Lysin |



|  |  |                       |                                                     |
|--|--|-----------------------|-----------------------------------------------------|
|  |  | Tamper                | Polypropylen                                        |
|  |  | Pusher                | Edelstahl 304V                                      |
|  |  | Schieber              | Polybutylenterephthalat (PBT)                       |
|  |  | Gehäuse               | Polybutylenterephthalat (PBT)                       |
|  |  | Taste                 | Polybutylenterephthalat (PBT)                       |
|  |  | Tastendeckel          | Polyoxymethylen (POM)/Polyacetal-Copolymer          |
|  |  | Manschette            | Polybutylenterephthalat (PBT)                       |
|  |  | Distanzstück          | Polybutylenterephthalat (PBT)                       |
|  |  | Kegel                 | Polypropylen                                        |
|  |  | Gehäusedeckel         | Polybutylenterephthalat (PBT)                       |
|  |  | Sicherheitsverschluss | Polybutylenterephthalat (PBT),<br>Blaupigment       |
|  |  | Manschettedeckel      | Polybutylenterephthalat (PBT)                       |
|  |  | Schlauchdichtung      | Silikon, Shore A 70                                 |
|  |  | Gehäusedichtung       | Silikon, Shore A 50                                 |
|  |  | Feder                 | Edelstahl 302                                       |
|  |  | Kegelschleuse         | Polypropylen<br>Silikon (Dow Corning 360),<br>Hexan |

\*Implantierbarer Teil des Produkts; die implantierbaren Komponenten sind MRT-sicher

Das FemoSeal™ VCS wurde mittels Ethylenoxid (EO) sterilisiert und ist ein Medizinprodukt für den Einmalgebrauch. Das FemoSeal™ VCS ist so konzipiert, dass es nicht wiederverwendet werden kann.

**Wirkungsweise**

Das FemoSeal™ VCS fördert die mechanische Hämostase, indem implantierbare Verschlusselemente innerhalb und außerhalb der A. femoralis communis platziert werden. Der Mechanismus zur Verhinderung von Blutungen wird durch die Innendichtung, die die Punktionsstelle abdichtet, und die äußere Sperrscheibe, die die Innendichtung in Position hält, gewährleistet.

### 1.2.3 Klinischer Nutzen

Das FemoSeal™ VCS bietet folgenden klinischen Nutzen beim Gefäßverschluss nach Punktionen der A. femoralis communis:

- Verkürzung der Zeit bis zur Hämostase<sup>1</sup>
- Verkürzung der Zeit bis zur Mobilisierung<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, S. 32–44.

### 1.2.4 Vorherige Generation(en) oder Varianten

- Die erste Version des FemoSeal™ VCS (Nr. 11200) wurde 2005 und teilweise 2006 auf dem europäischen Markt verkauft.
- Das aktuelle FemoSeal™ VCS (Nr. 11202) mit verbessertem Applikationssystem ist seit dem 28. März 2006 auf dem Markt.

### 1.2.5 Zubehör zur Verwendung in Kombination mit dem Produkt

Die FemoSeal™ Einheit wird zusammen mit einem Dilatator und einem Führungsdraht mit 0,038" (0,97 mm) Außendurchmesser, 27,5" (70 cm) Länge sowie einer J-Spitze geliefert. Der Führungsdraht ist ein Zubehörteil der FemoSeal™ Einheit. Die J-Spitze ist eine Komponente des Führungsdrahts, während der Dilatator eine Komponente der FemoSeal™ Einheit ist. Der Führungsdraht ist das einzige Zubehör dieses Medizinprodukts. Der Führungsdraht befindet sich in einem Polyethylenschlauch. Alle Teile sind in einer stabilen Papierkassette verpackt. Die Verpackung enthält auch den Implantatausweis für den/die Patienten/Patientin. Das FemoSeal™ Vascular Closure System erfordert kein zusätzliches Zubehör, um wie vorgesehen zu funktionieren. Das Produkt ist nur für die Verwendung mit dem Dilatator und dem Führungsdraht vorgesehen, die in der Produktverpackung enthalten sind.

### 1.2.6 Andere Vorrichtungen und Produkte, die für die Verwendung in Kombination mit dem Produkt vorgesehen sind

Das FemoSeal™ VCS erfordert keine zusätzlichen Vorrichtungen, um wie vorgesehen zu funktionieren.

## 1.3 Risiken und Warnhinweise

### 1.3.1 Restrisiken und unerwünschte Wirkungen

Bekannte oder vorhersehbare unerwünschte Ereignisse, Probleme und Komplikationen im Zusammenhang mit der Verwendung des FemoSeal™ VCS als Folge von Restrisiken sind in **Tabelle 1.2** aufgeführt. Die Häufigkeitsrate basiert auf einer Analyse der Dokumentation zu Risiken und wurde auf der Grundlage von Überwachungsdaten nach dem Inverkehrbringen aus dem Zeitraum vom 1. September 2019 bis 31. August 2024 berechnet. Es gibt keine unbekannten Restrisiken für das FemoSeal™ VCS, und alle anwendbaren Risiken wurden durch die Bedienungsanleitung und den Risikomanagementprozess behandelt.

**Tabelle 1.2. FemoSeal™, unerwünschte Ereignisse/Komplikationen**

| Problem                   | Häufigkeitsrate (%) | Minderungsfaktoren                                                                                                                                                                            |
|---------------------------|---------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Allergische Reaktion      | 0,0000              | Maßnahmen und Pläne, um das Risiko so weit wie möglich zu reduzieren, wurden in Form von Produktdesignmerkmalen, Herstellungsrichtlinien, Produktbeschriftungen und Arztschulungen umgesetzt. |
| Aneurysma                 | 0,0000              |                                                                                                                                                                                               |
| AV-Fistel                 | 0,0001              |                                                                                                                                                                                               |
| Blutverlust/Blutung       | 0,0280              |                                                                                                                                                                                               |
| Tod                       | 0,0002              |                                                                                                                                                                                               |
| Ekchymose                 | 0,0000              |                                                                                                                                                                                               |
| Embolie                   | 0,0000              |                                                                                                                                                                                               |
| Fremdkörperabwehrreaktion | 0,0000              |                                                                                                                                                                                               |
| Hämatom                   | 0,0027              |                                                                                                                                                                                               |
| Blutung                   | 0,0001              |                                                                                                                                                                                               |
| Infektion                 | 0,0002              |                                                                                                                                                                                               |
| Entzündungsreaktion       | 0,0000              |                                                                                                                                                                                               |
| Taubheitsgefühl           | 0,0000              |                                                                                                                                                                                               |
| Schmerzen                 | 0,0000              |                                                                                                                                                                                               |
| Unwohlsein des Patienten  | 0,0004              |                                                                                                                                                                                               |
| Eingriffsverzögerung      | 0,0065              |                                                                                                                                                                                               |
| Pseudoaneurysma           | 0,0004              |                                                                                                                                                                                               |
| Retroperitoneale Blutung  | 0,0002              |                                                                                                                                                                                               |
| Sepsis                    | 0,0000              |                                                                                                                                                                                               |

| Problem                                          | Häufigkeitsrate (%) | Minderungsfaktoren |
|--------------------------------------------------|---------------------|--------------------|
| Thromboembolie                                   | 0,0000              |                    |
| Thrombose                                        | 0,0001              |                    |
| Gefäßokklusion/Ischämie der unteren Extremitäten | 0,0002              |                    |
| Gefäßperforation                                 | 0,0000              |                    |
| Dissektion/Lazeration des Gefäßgewebes           | 0,0003              |                    |

### 1.3.2 Warnhinweise und Sicherheitsmaßnahmen

#### Warnhinweise

1. Nicht verwenden, wenn die Verpackung beschädigt oder eine Sterilbarriere nicht intakt ist.
2. Nicht nach Ablauf des Verfallsdatums verwenden, da die biologisch abbaubaren Komponenten dann eventuell nicht mehr wie vorgesehen funktionieren.
3. Nicht verwenden, wenn Elemente beschädigt oder in irgendeiner Weise defekt erscheinen.
4. Wenn die Prozedurschleuse oder das umgebende Gewebe bakteriell kontaminiert sind, kann die Verwendung des FemoSeal™ Vascular Closure Systems eine Infektion verursachen.
5. Wenn vermutet wird, dass die hintere Arterienwand punktiert wurde, oder wenn mehr als eine arterielle Punktion vorgenommen worden ist, sollte nicht allein auf das FemoSeal™ Vascular Closure System zurückgegriffen werden, um eine arterielle Hämostase zu erreichen. Setzen Sie in diesem Fall zusätzliche manuelle oder mechanische Kompression ein.
6. Wenn die arterielle Punktionsstelle an oder distal der Bifurkation der A. femoralis liegt, sollte das FemoSeal™ Vascular Closure System nicht verwendet werden. In diesem Fall besteht die Gefahr, dass sich die Innendichtung nicht korrekt positionieren lässt. Ein solches Ereignis wiederum könnte zu einer Blutungskomplikation und/oder zu einer Unterbrechung des normalen Blutflusses führen.
7. Wenn eine persistierende arterielle Blutung am Ort der Inzision besteht, darf das Multifilament nicht gekappt werden, bevor die Blutung gestillt ist. Wenn keine Hämostase erreicht wird, befestigen Sie das Multifilament mit einem sterilen Wundverband und ergreifen Sie zusätzliche Maßnahmen zur Kompression, bis die

Hämostase erreicht ist. Bei einer persistierenden arteriellen Blutung können erhebliche Blutungskomplikationen auftreten, die zu Verletzungen oder zum Tod des Patienten führen können.

8. Verwenden Sie das FemoSeal™ Vascular Closure System nicht, wenn sich die Punktionsstelle in der Nähe des Ligamentum inguinale befindet, da dies zu einem retroperitonealen Hämatom führen kann.
9. Bei Patienten mit einem höheren Blutungsrisiko kann es zu einem verstärkten Blutverlust kommen, der eine Transfusion erfordert.
10. Wenn sich die Innendichtung löst, kann dies ein thrombotisches und/oder embolisches Ereignis verursachen.

### **Vorsichtsmaßnahmen**

1. Das Einsetzen des FemoSeal™ Vascular Closure Systems sollte ausschließlich von Ärzten durchgeführt werden, die im Einsatz des Systems entsprechend geschult wurden.
2. Führen Sie vor dem Einsetzen des FemoSeal™ Vascular Closure Systems ein begrenztes femorales Angiogramm oder eine ultraschallgeführte femorale Punktion durch.
3. Brechen Sie den Eingriff unter folgenden Umständen ab:
  - Der Lumendurchmesser der A. femoralis communis ist kleiner als 5 mm.
  - Es befinden sich eine Stenose und/oder signifikante Plaque in der Nähe der gemeinsamen Punktionsstelle der A. femoralis communis.
  - Die Punktionsstelle befindet sich an oder distal der Bifurkation der A. femoralis.
  - Es befinden sich abnorme Verzweigungen oder Gefäßanomalien in der Nähe der Punktionsstelle der A. femoralis communis.
4. Wenn ein Hämatom vorhanden ist, muss besonders darauf geachtet werden, dass die Kegelschleuse korrekt in die Arterie eingeführt wird.
5. Punktieren Sie einwandig. Punktieren Sie nicht die posteriore Arterienwand.
6. Bei der Verwendung des FemoSeal™ Vascular Closure Systems sind stets sterile Verfahren einzuhalten.
7. Das FemoSeal™ Vascular Closure System ist nur zum einmaligen Gebrauch bestimmt und darf nicht wiederverwendet oder erneut sterilisiert werden. Die FemoSeal™ Einheit ist so konzipiert, dass sie nicht wiederverwendet werden kann.
8. Wenn Sie beim Einsetzen der Innendichtung auf einen unerwarteten Widerstand stoßen, muss der Vorgang abgebrochen werden.

9. Um die Innendichtung richtig einzusetzen, positionieren Sie Ihren Daumen so, dass die Taste frei zurückfedern kann.
10. Stellen Sie sicher, dass sich die Spitze der Kegelschleuse der FemoSeal™ Einheit unter der Hautoberfläche befindet, bevor Sie die äußere Sperrscheibe befestigen. Bei Patienten mit kurzem Abstand zwischen der A. femoralis und der Hautoberfläche kann es zu einer unbeabsichtigten Festsetzung der äußeren Sperrscheibe über dem Hautlevel kommen.
11. Für eine korrekte Platzierung muss eventuell vor dem Einsetzen eine Hautinzision durchgeführt werden.
12. Wenn sich die Innendichtung in der Arterie befindet und es dennoch nicht möglich ist, die Verschluss Taste vollständig zu drücken und die äußere Sperrscheibe zu befestigen, muss eventuell ein chirurgischer Eingriff vorgenommen werden, um die FemoSeal™ Verschlusselemente zu entfernen.
13. Falls innerhalb von 18 Monaten eine erneute Punktion derselben A. femoralis erforderlich wird, ist diese mindestens einen Zentimeter proximal zur ersten Zugangsstelle des FemoSeal™ Vascular Closure Systems auszuführen.
14. Weisen Sie den Patienten/die Patientin an, sich genau an die ärztlichen Anweisungen zur Inspektion der Verschlussstelle zu halten.
15. Weisen Sie den Patienten/die Patientin an, die Patienteninformationskarte für die nächsten 18 Monate mitzuführen.

### **Vorsichtsmaßnahmen bei der Entlassung**

Untersuchen Sie den Patienten/die Patientin vor seiner/ihrer Entlassung auf folgende klinische Symptome:

1. Blutung und/oder Hämatom an der Verschlussstelle.
2. Schmerzen beim Gehen.
3. Entzündungszeichen an der Verschlussstelle.

### **1.3.3 Sicherheitsmaßnahmen im Feld**

Im Zeitraum vom 1. September 2019 bis zum 31. August 2024 gab es eine Sicherheitsmaßnahme im Feld, die das FemoSeal™ VCS betraf.

Im Jahr 2022 hat Terumo FemoSeal™ VCS freiwillig zurückgerufen, da Beschwerden eingereicht wurden, in denen Fehler bei Prozess- und Losfreigabeproofungen in von Elcton hergestellten FemoSeal-Produkten zur Messung der Stampfkraft und der Rückzugskraft gemeldet wurden. Insgesamt wurden 950 Einheiten aus Südkorea zurückgerufen.

## 1.4 Zusammenfassung der klinischen Bewertung und der klinischen Nachbeobachtung nach dem Inverkehrbringen

**Tabelle 1.3** enthält eine Liste der Zulassungsstudien, die für die Markteinführung von FemoSeal™ VCS durchgeführt wurden, sowie der Studien und der klinischen Nachbeobachtungen nach dem Inverkehrbringen. Die in der Studie verwendete Produktversion ist in der folgenden Tabelle aufgeführt. Die erste Version des FemoSeal™ VCS (Nr. 11200) war bis 2006 auf dem Markt, die Nachfolgeversion (Nr. C11202) wurde 2006 auf den Markt gebracht und ist bis heute erhältlich.

**Tabelle 1.3 Zusammenfassung der Zulassungsstudien**

| <b>Funktionelle Tierversuche vor dem Inverkehrbringen</b>                                                                                                                                                                                                               | <b>Produktversion</b>      |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                      |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                      |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                      |
| <b>Erste klinische Humanstudie</b>                                                                                                                                                                                                                                      |                            |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                      |
| <b>Abgeschlossene klinische Studien nach dem Inverkehrbringen</b>                                                                                                                                                                                                       |                            |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                                                                              | C11202 (aktuelles Produkt) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                                                                                       | C11202 (aktuelles Produkt) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                                                                                                                                                          | C11202 (aktuelles Produkt) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)                                                                                                                                                  | C11202 (aktuelles Produkt) |
| <b>Geplante/laufende klinische Studien nach dem Inverkehrbringen</b>                                                                                                                                                                                                    |                            |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                                                                                                                                                              | C11202 (aktuelles Produkt) |
| <b>Klinische Nachbeobachtungen nach dem Inverkehrbringen</b>                                                                                                                                                                                                            |                            |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                                                                                                                                                               | C11202 (aktuelles Produkt) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                                                                                                                                                                      | C11202 (aktuelles Produkt) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024)                                                                                                                                         | C11202 (aktuelles Produkt) |

### 1.4.1 Zusammenfassung der Daten vor dem Inverkehrbringen (aus Tierversuchen und klinischen Untersuchungen)

In der nachstehenden **Tabelle 1.4** sind alle Studien vor dem Inverkehrbringen beschrieben, sowohl Tierversuche als auch klinische Studien.

**Tabelle 1.4 Zusammenfassungen von Studien vor dem Inverkehrbringen**

| Funktionelle Tierversuche vor dem Inverkehrbringen                                                                                                                                                                                                                      |                                                                              |                                      |                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|--------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Name der Studie                                                                                                                                                                                                                                                         | Jahr/CI                                                                      | Art der Studie                       | Ziele                                                                                                                                                                                                                                                                   | Meilensteine                                                                                                                                                                                                                                                                                                                                                                               | Mögliche Akzeptanzkriterien                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 2000<br>Radi Medical System AB<br><br>Durchgeführt von Biomatech, Frankreich | Tierstudie, explorative Untersuchung | Ziel der Studie war es, die Biokompatibilität und Biofunktionalität eines biologisch abbaubaren Implantats zu bewerten, das entwickelt wurde, um eine Hämostase im Gefäßsystem zu erreichen. Der Bericht betrifft Reservetiere aus Studie Nr. 862 (Dokumentnr. 1051-01) | N = 3 erwachsene weibliche Schafe, 1 Tier pro Zeitpunkt<br><br>Nachbeobachtung zur histopathologischen Analyse, makroskopischen Einstufung und ultrastrukturellen Analyse<br><br><ul style="list-style-type: none"> <li>12 Monate</li> <li>15 Monate</li> <li>18 Monate</li> </ul> Farbdoppler-Ultraschall-Nachbeobachtung – 30 Tage an Zugangsstellen der A. femoralis und der A. carotis | Arterielle Durchgängigkeit <ul style="list-style-type: none"> <li>Beurteilung des Blutflusses nach dem Einsetzen – 2/3 Verringerung des Blutflusses im Zusammenhang mit vorübergehendem arteriellen Vasospasmus, der dem Eingriff zugeschrieben wurde, beide traten an der linken A. carotis communis auf</li> <li>Farbdoppler-Ultraschalluntersuchung (4 Wochen) – 3/3 (100 %) ohne größere Reduzierung des Blutflusses 30 Tage nach der Implantation</li> </ul> Makroskopische Beobachtungen <ul style="list-style-type: none"> <li>12 Monate – Durchgängigkeit makroskopisch bestätigt durch Abwesenheit eines anatomisch sichtbaren Verschlusses, keine makroskopischen lokalen Unverträglichkeitsläsionen (Blutungen, Nekrosen oder Neovaskularisationen), Verkapselung der Innenscheibe schien ausgeprägt zu sein</li> <li>15 Monate – Makroskopische Beobachtung ergab keine Anzeichen einer Entzündung, es wurden keine Rückstände der Innen- oder Außenscheibe festgestellt, das Erscheinungsbild des</li> </ul> |



|                                                                                                                 |                             |                                      |                                                                                                                            |                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|-----------------------------------------------------------------------------------------------------------------|-----------------------------|--------------------------------------|----------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                 |                             |                                      |                                                                                                                            |                                                                                                                                       | <p>Einkapselungsgewebes im Bereich der Außenscheibe war im Vergleich zur Beobachtung nach 12 Monaten unverändert</p> <ul style="list-style-type: none"> <li>18 Monate – Makroskopische Beobachtung ergab keine Anzeichen lokaler Intoleranz, Außenscheibe sichtbar (3/3 Fälle), Abbau der Innenscheibe abgeschlossen; 1/3 (linke A. carotis communis) – Depression der Arterienwand an der Implantationsstelle beobachtet (könnte mit der Platzierung des Produkts zusammenhängen)</li> </ul> <p>Schlussfolgerungen</p> <ul style="list-style-type: none"> <li>Makroskopisch wurden 12, 15 und 18 Monate nach der Implantation keine nekrotischen, degenerativen oder thrombotischen Anzeichen festgestellt.</li> <li>Der Abbauprozess der Innen- und der Außenscheibe schien zwischen 12 und 18 Monaten voranzuschreiten und nach 18 Monaten abgeschlossen zu sein, wobei ein weißliches Gewebe den implantierten Bereich bedeckte.</li> <li>Histologisch war nach 18 Monaten kein Polymermaterial mehr sichtbar, sondern ein endoluminales fibröses Gewebe vorhanden. Es wurden keine nekrotischen, degenerativen oder thrombotischen Läsionen festgestellt.</li> </ul> |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. | 2002 Radi Medical System AB | Tierstudie, explorative Untersuchung | Ziel der Studie war es, die Biokompatibilität eines biologisch abbaubaren Implantats zu bewerten, das entwickelt wurde, um | Nachbeobachtung (nach Implantation) <ul style="list-style-type: none"> <li>12 Wochen</li> <li>24 Wochen</li> <li>36 Wochen</li> </ul> | <u>Durchgängigkeit der A. femoralis und der A. carotis communis nach 4 Wochen</u>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |

|                                                                                                                                                         |                                        |  |                                             |                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|--|---------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | Durchgeführt von Biomatech, Frankreich |  | eine Hämostase im Gefäßsystem zu erreichen. | <p>N = 12 Schafe, 3 Tiere pro Zeitpunkt, 3 Reservetiere, getötet nach 12, 15 und 18 Monaten</p> <p>Implantationsstellen: rechte und linke A. femoralis, rechte und linke A. carotis communis</p> <p>Farbdoppler-Ultraschallanalyse</p> | <ul style="list-style-type: none"> <li>• Erhebliche Verringerung des Blutflusses 0/12 (0 %)</li> </ul> <p><u>Keine signifikante Verringerung des Blutflusses</u></p> <ul style="list-style-type: none"> <li>• Schwere Beeinträchtigung des Blutflusses im Zusammenhang mit dem Einführen des Produkts 0/12 (0 %)</li> <li>• Verringerung des Blutflusses in der linken A. carotis communis 2/12 (16,6 %) aufgrund eines vorübergehenden arteriellen Vasospasmus (auf die Operation zurückzuführen, nicht auf das Produkt)</li> </ul> <p><u>Beeinträchtigung des Blutflusses bei der Nachbeobachtung</u></p> <p>12 Wochen – 0/12 (0 %)<br/> 24 Wochen – 0/12 (0 %)<br/> 36 Wochen – 0/12 (0 %)</p> <p>Blutdruckmessungen (3 Schafe – 36 Wochen)</p> <ul style="list-style-type: none"> <li>• Keine signifikante Verringerung des Blutflusses festgestellt</li> </ul> <p>Makroskopische Daten für Integration und Degradation (Grad 0–4)</p> <p><u>Zugangstellen A. carotis Innenseite</u></p> <p>- Einkapselung<br/> 12 Wochen – 1,3<br/> 24 Wochen – 0,8<br/> 36 Wochen – 0,7</p> <p>- Materialabbau<br/> 12 Wochen – 2,2<br/> 24 Wochen – 2,3<br/> 36 Wochen – 0,7</p> <p><u>Außenseite</u></p> <p>- Einkapselung<br/> 12 Wochen – 2,0<br/> 24 Wochen – 1,0</p> |
|---------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|--|---------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | 36 Wochen – 0,8<br>- Materialabbau<br>12 Wochen – 2,0<br>24 Wochen – 2,7<br>36 Wochen – 3,2<br><br><u>Zugangstellen A. femoralis</u><br><u>Außenseite</u><br>- Einkapselung<br>12 Wochen – 1,0<br>24 Wochen – 2,7<br>36 Wochen – 1,0<br>- Materialabbau<br>12 Wochen – 2,0<br>24 Wochen – 2,4<br>36 Wochen – 3,0<br><br><u>Innenseite</u><br>- Einkapselung<br>12 Wochen – 2,0<br>24 Wochen – 1,2<br>36 Wochen – 1,0<br>- Materialabbau<br>12 Wochen – 1,0<br>24 Wochen – 2,2<br>36 Wochen – 3,0<br><br><u>Histologische Daten für</u><br><u>Integrations-, Abbau- und</u><br><u>Entzündungsparameter (Mittel</u><br><u>der relevanten Werte, Index</u><br><u>0–4) n = 6</u><br><br><u>Zugangstellen A. carotis</u><br>Externe Fibrose<br>12 Wochen – 2,3<br>24 Wochen – 2,3<br>36 Wochen – 1,8<br>Interne Neointimabildung<br>12 Wochen – 3,0<br>24 Wochen – 2,7<br>36 Wochen – 3,3<br>Materialabbau<br>12 Wochen – 1,7<br>24 Wochen – 3,0<br>36 Wochen – 3+<br>Entzündungsparameter<br>(Makrophagen)<br>12 Wochen – 3,0<br>24 Wochen – 1,7<br>36 Wochen – 1,7 |
|--|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | <u>Zugangstellen A. femoralis</u><br>Externe Fibrose<br>12 Wochen – 1,3<br>24 Wochen – 1,5<br>36 Wochen – 1,7<br>Interne Neointimabildung<br>12 Wochen – 3,7<br>24 Wochen – 3,3<br>36 Wochen – 3,8<br>Materialabbau<br>12 Wochen – 2,0<br>24 Wochen – 3,0<br>36 Wochen – 3+<br>Entzündungsparameter (Makrophagen)<br>12 Wochen – 3,5<br>24 Wochen – 1,8<br>36 Wochen – 1,8<br><br><u>Histomorphologische Durchgängigkeitswerte</u><br>Zugangstellen A. carotis<br>12 Wochen – 74,0 %<br>24 Wochen – 81,9 %<br>36 Wochen – 89,43 %<br>Zugangstellen A. femoralis<br>12 Wochen – 42,2 %<br>24 Wochen – 73,21 %<br>36 Wochen – 78,71 %<br><br><u>US-Gefäßdurchgängigkeit (Mittelwert %)</u><br>Zugangstellen A. carotis<br>12 Wochen – 94,6 %<br>24 Wochen – 96,7 %<br>36 Wochen – 94,7 %<br>Zugangstellen A. femoralis<br>12 Wochen – 66,9 %<br>24 Wochen – 63,6 %<br>36 Wochen – 75,1 %<br><br>Schlussfolgerungen <ul style="list-style-type: none"> <li>• Es wurde kein signifikantes lokales Intoleranzzeichen (Fehlen sichtbarer entzündlicher, nekrotischer oder degenerativer Läsionen) nach 12, 24 oder 36 Wochen festgestellt</li> <li>• Es wurden keine signifikanten</li> </ul> |
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|                                                                                                                                                                                                                                                                        |                                                                                         |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                         | unerwünschten Gewebereaktionen in Bezug auf den Träger/die Trägerin und das Produkt festgestellt                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                                                                                        |                                                                                         |                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                         | <ul style="list-style-type: none"> <li>Der Abbau des Implantats war nach 36 Wochen beinahe abgeschlossen</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002</p> <p>Radi Medical System AB</p> <p>Durchgeführt von Biomatech, Frankreich</p> | <p>Tierstudie</p> | <p>Ziel der Studie war es, die Biokompatibilität und Biofunktionalität eines biologisch abbaubaren Implantats zu bewerten, das entwickelt wurde, um eine Hämostase im Gefäßsystem zu erreichen. Das geprüfte Produkt sollte in die Punktieröffnung der Arterien eindringen, um eine Hämostase zu erreichen. Eine Scheibe trat in die Punktionsöffnung in der Arterie ein, die andere zog die Innenscheibe von außerhalb der Arterie an. Beide Scheiben wurden durch eine Einführschleuse eingeführt. Die Scheiben wurden so konzipiert, dass sie Blutungen verhindern, in die Gefäßwand einheilen und schließlich abgebaut und resorbiert werden. Die Studie diente der Erfassung und Analyse von Daten nach funktioneller Implantation in Schafen und in einem Schwein, um die Fähigkeit des Implantats zur Aufrechterhaltung der physiologischen Funktion bei Verwendung im Kreislaufsystem zu bewerten, die Reaktion des Wirts und die Reaktion des Produkts</p> | <p>Implantationszeitraum/Nachbeobachtung beträgt 5 Wochen für alle Tiere</p> <p>4 Schafe, 1 Schwein</p> <p>14 Verschlusselemente</p> <p>8 Verschlusselemente in 2 Schafen implantiert,</p> <p>2 Verschlusselemente in 1 Schwein implantiert</p> <p>Wenn zwei Verschlusselemente in dieselbe A. femoralis implantiert wurden, wurden sie in einem Abstand von &gt; 30 mm implantiert</p> | <p>Alle unerwünschten Anzeichen (Entzündungen, Nekrosen, Blutungen oder andere Läsionen) oder die Bildung einer dünnen pseudo-intimalen Schicht wurden erfasst. Besondere Aufmerksamkeit wurde der anfänglichen geweblichen Integration des Produkts gewidmet, mit besonderem Augenmerk auf die Verkapselung der Innenscheibe.</p> <p>Makroskopisch wurden keine signifikanten Anzeichen einer lokalen Intoleranz oder Thrombusbildung beobachtet. Die makroskopische Beobachtung ergab keinen Unterschied zwischen Schaf und Schwein nach der Implantation der Verschlusselemente in die A. femoralis.</p> <p>Makroskopisch wurden keine signifikanten Anzeichen einer lokalen Intoleranz oder Thrombusbildung beobachtet. Die makroskopische Beobachtung ergab keinen Unterschied zwischen Schaf und Schwein nach der Implantation der Verschlusselemente in die A. femoralis.</p> |

|  |  |  | (körperliche Unversehrtheit, gewebliche Verkapselung bei der Tötung) zu bestimmen und die Degradation des Implantats zu bewerten |  | <p>Die histopatologische Analyse der Implantationsstelle bei Schafen ergab keine lokalen Nebenwirkungen. Die Innen- und Außenscheiben zeigten Anzeichen von Degradation und waren in einigen Fällen in kleinere Teile zerbrochen. Die Innenscheiben waren vollständig in das neointimale Gewebe integriert. Bei dem Schwein zeigte die histopatologische Analyse etwas mehr Entzündungszeichen um die Innen- und Außenscheibe. Bei beiden Tierrgattungen wies das Multifilament etwas mehr Entzündungszeichen auf als das Scheibenmaterial, was bei geflochtenem Nahtmaterial aufgrund der größeren Oberfläche normal ist.</p> <p>Die Durchgängigkeit der Gefäße wurde nach 5 Wochen mit drei verschiedenen Methoden gemessen: histomorphometrisch, histomorphometrisch in Kombination mit der Messung des Gefäßdurchmessers mit einer Schieblehre und mit Farbdoppler-Sonographie. Die mittlere Gefäßdurchgängigkeit bei den Schafen lag je nach Methode zwischen 60 und 80 % (12 Beobachtungen). Beim Schwein lag die mittlere</p> |
|--|--|--|----------------------------------------------------------------------------------------------------------------------------------|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                                                                                                                                                                                                              |                              |                                               |                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                            | Gefäßdurchgängigkeit zwischen 40 und 80 % (2 Beobachtungen).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
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| <b>Erste klinische Humanstudie</b>                                                                                                                                                                           |                              |                                               |                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Name der Studie                                                                                                                                                                                              | Jahr/CI                      | Art der Studie                                | Ziele                                                                                                                                                                                                                                                                                                                                                     | Meilensteine                                                                                                                                                                                                                                                                                                                                                                                                                               | Mögliche Akzeptanzkriterien                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Einarmige, multizentrisch e Open-Label-Studie | Ziel der Studie war es, die Sicherheit, Leistungsfähigkeit und Effektivität des FemoSeal Vascular Closure Systems (FemoSeal System) im Allgemeinen und der Verschlusselemente im Besonderen bei Patienten zu untersuchen, die sich einem diagnostischen oder interventionellen kardiologischen Verfahren über einen femoralen Arterienzugang unterziehen. | Zweiteilige Studie<br><br>Gesamt n = 80<br>Abschnitt 1: n = 20<br>Abschnitt 2 n = 60<br>Indikationen:<br>Abschnitt 1: Diagnostische Herzkatheterisierung unter Verwendung der Oberschenkelarterie als Zugangsstelle<br><br>Abschnitt 2: Patienten, die sich diagnostischen und interventionellen kardialen Eingriffen unterziehen, bei denen die Oberschenkelarterie als Zugangsstelle verwendet wird<br><br>Nachbeobachtung nach 30 Tagen | Ergebnisse<br><u>- Hämostase mit FS ohne Kompression erreicht</u><br>- Abschnitt 1 20/20 (100 %)<br>- Abschnitt 2 58/60 (97 %)<br>Mediane Zeit bis zur Hämostase zum Zeitpunkt des Eingriffs (Teil 2): 1,0 Minuten (Bereich unmittelbar – 8 Minuten)<br><br><u>Zeit bis Mobilisierung (Minuten)</u><br>Abschnitt 1 – Median: 33,0<br>Durchschnitt: 67,8<br>Abschnitt 2 – Median: 45<br>Durchschnitt: 87,5<br><br><u>Inzidenz schwerer vaskulärer Komplikationen – Nachbeobachtung nach 30 Tagen</u><br>Abschnitt 1<br>- Ohne vaskuläre Komplikationen 20/20 (100 %)<br>Abschnitt 2<br>Pseudoaneurysma – 1/59 (1,69 %)<br><br><u>Behandlungsversagen</u><br>Abschnitt 1 – 0/20 (0 %)<br>Abschnitt 2 – 3/60 (5 %) |

|  |  |  |  |  | <ul style="list-style-type: none"> <li>• 2 aufgrund fehlender Hämostase ohne Anwendung von Kompression</li> <li>• 1 aufgrund einer schweren vaskulären Komplikation, Pseudoaneurysma</li> </ul> <p><u>Anhaltende Sickerblutungen</u></p> <p>Abschnitt 1 – 0/20 (0 %)</p> <p>Abschnitt 2 – 8/60 (13 %)</p> <p><u>Hämatome</u></p> <p>Abschnitt 1 – 0/20 (0 %)</p> <p>Abschnitt 2 – 6/60 (10 %)</p> |
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Im Rahmen des Entwicklungsplans für FemoSeal™ VCS vor dem Inverkehrbringen wurden drei Funktionstests an Tieren durchgeführt. Im Jahr 2000 wurde vor Beginn der klinischen Studien eine Tierstudie zur Bewertung der Biofunktionalität von FemoSeal™ VCS durchgeführt. In dieser Studie wurde der Abbau der Verschlusselemente beurteilt sowie deren Fähigkeit, die physiologische Funktion aufrechtzuerhalten. Nach 18 Monaten war das Material der Innen- und der Außenscheibe nicht mehr sichtbar, da es durch ein endoluminales fibröses Gewebe ersetzt worden war. Zusammenfassend lässt sich sagen, dass die Fähigkeit des FemoSeal™ VCS Verschlusselements zur Aufrechterhaltung der physiologischen Funktion bei Verwendung im Kreislaufsystem bestätigt wurde.

Im Jahr 2002 wurde eine Tierstudie durchgeführt, um die Biokompatibilität und Biofunktionalität eines biologisch abbaubaren Implantats, des FemoSeal™ VCS, zu untersuchen, das für die Hämostase im Gefäßsystem entwickelt wurde. Zusammenfassend lässt sich sagen, dass der Abbau des Implantats innerhalb von 36 Wochen nahezu abgeschlossen war und keine signifikanten unerwünschten Gewebereaktionen auftraten.

Eine weitere Tierstudie aus dem Jahr 2002 untersuchte die Biokompatibilität und Biofunktionalität eines biologisch abbaubaren Implantats, des FemoSeal™ VCS, das für die Hämostase im Gefäßsystem entwickelt wurde. Nach 5 Wochen war die Einkapselung der Innenscheibe abgeschlossen, und es wurden Anzeichen von Degradation bei der Innen- und der Außenscheibe beobachtet. Zusammenfassend wurde die Fähigkeit des Implantats zur Aufrechterhaltung der physiologischen Funktion beim Einsatz im Kreislaufsystem bestätigt.



Im Rahmen des klinischen Entwicklungsplans für das FemoSeal™ VCS hat Radi Medical System AB eine klinische Studie vor dem Inverkehrbringen durchgeführt. Diese klinische Studie ist weder veröffentlicht noch online verfügbar. Die Studie mit dem Produktmodell Nr. 11200 wurde 2002–2004 gemäß der Europäischen Norm EN 540 (Klinische Prüfung von Medizinprodukten an Menschen) und in Übereinstimmung mit den ICH General Considerations for Clinical Trials und der Guideline for Good Clinical Practice durchgeführt. Die Details dieser Studie sind im Bericht EU-SE-001 dokumentiert. Die klinische Prüfung wurde im Abschlussbericht von Radi Medical Systems AB, „Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures“, dokumentiert. Die klinische Studie wurde mit der ersten FemoSeal™-Version Nr. 11200 durchgeführt und konzentrierte sich auf die Sicherheit und Wirksamkeit der implantierbaren Verschlusskomponenten. Der einzige Unterschied zwischen der ersten Version Nr. 11200 und der aktuellen Version Nr. C11202 ist die französische Größe, 6F bzw. 7F, und das verbesserte Applikationssystem. Der klinische Nutzen, der Verwendungszweck, die Funktionsprinzipien und die Ausgangsmaterialien der implantierbaren Verschlusselemente, der Innendichtung und der äußeren Sperrscheibe, sind unverändert.

Das Produkt war für Patienten bestimmt, die sich diagnostischen oder interventionellen kardiologischen Verfahren unter Verwendung der Oberschenkelarterie als Zugangsstelle unterziehen. Ziel dieser Studie war es, die Sicherheit, Leistung und Wirksamkeit des FemoSeal™ VCS zu bestimmen. Es handelte sich um eine prospektive, multizentrische, einarmige Open-Label-Studie mit einer Nachbeobachtung nach 30 Tagen.

Der primäre Leistungsendpoint war die Zeit bis zur Hämostase, definiert als das Ausbleiben von Blutungen. Der primäre Sicherheitsendpoint war die Inzidenz schwerer vaskulärer Komplikationen innerhalb von 30 Tagen nach dem Eingriff. Sekundäre Endpunkte waren die Zeit bis zur Mobilisierung, der Anteil der Behandlungsversagen, die Inzidenz unerwünschter Ereignisse und die Leistungsmerkmale des Produkts während der Applikation und des Einsetzens.

Die in diese Studie aufgenommenen Patienten waren Erwachsene, die in der Lage waren, eine Einwilligungserklärung abzugeben und mindestens einen intakten Pedalpuls hatten. Die Patienten wurden von der Studie ausgeschlossen, wenn sie an einer der folgenden Erkrankungen litten:

- Vorgeschichte einer peripheren Gefäßerkrankung
- Autoimmunerkrankung
- Bekannte Blutungsstörung oder schwere Anämie
- INR > 1,5
- Myokardinfarkt innerhalb von 72 Stunden

- Unkontrollierte Hypertonie trotz Behandlung
- Adipositas, die einen Zugang mithilfe der Seldinger-Technik ausschließt
- Vorhandensein eines Gefäßersatzes oder Stents an der Arteriotomiestelle
- Vorheriges ipsilaterales Punktieren innerhalb von 3 Monaten
- Lebenserwartung < 6 Monate

Darüber hinaus wurden die Patienten intraoperativ untersucht und aus der Studie ausgeschlossen, wenn eines der folgenden Merkmale festgestellt wurde:

- Lumendurchmesser der A. femoralis communis < 5 mm
- Arterienäste innerhalb von 2 cm proximal der Punktionsstelle
- Signifikante Stenose innerhalb von 3 cm der Punktionsstelle
- Verwendung einer Haupteinführschleuse > 6 Fr
- Punktion an oder distal der femoralen Bifurkation
- Mehrere femorale Punktionen
- Bekanntes oder vermutete Punktion der posterioren Femurwand
- Großes Hämatom (2:6 cm) nach Abschluss des Eingriffs
- Schwieriges Einführen der Primärschleuse bei Verfahren aufgrund von gewundenem Gewebe oder Gefäß

Diese Einzelprotokollstudie wurde in zwei Abschnitten durchgeführt: In Abschnitt 1 wurden 20 Patienten aufgenommen, dann wurde eine Sicherheitsanalyse durchgeführt, und in Abschnitt 2 wurden weitere 60 Patienten aufgenommen.

In Abschnitt 1 betrug das Durchschnittsalter der aufgenommenen Patienten 65,9 Jahre, 70,0 % der Patienten waren männlich und 95 % der Patienten erhielten Begleitmedikamente. In Abschnitt 2 der Studie lag das Durchschnittsalter bei 63,8 Jahren, 78 % waren männlich und 100 % der Patienten erhielten Begleitmedikamente.

Patienten, die sich einer diagnostischen (Abschnitt 1 und Abschnitt 2) oder interventionellen (Abschnitt 2) Herzkatheteruntersuchung unterzogen, konnten in die Studie aufgenommen werden. Die Verfahren entsprachen der Standardversorgung in jedem der teilnehmenden Krankenhäuser, gefolgt vom Einsatz des FemoSeal™ VCS. Die Patientendaten wurden zu Studienbeginn, während des Eingriffs sowie 1 Tag und 30 Tage nach dem Eingriff erhoben. Die Ergebnisse sind in **Tabelle 1.5** zusammengefasst und zeigen, dass das FemoSeal™ VCS für die Anwendung bei dieser Patientengruppe sicher und wirksam ist.

**Tabelle 1.5 Klinische Ergebnisse aus der Studie vor dem Inverkehrbringen**

|                                                                                                                             | Abschnitt 1  | Abschnitt 2               |
|-----------------------------------------------------------------------------------------------------------------------------|--------------|---------------------------|
| Anzahl der Patienten                                                                                                        | 20           | 60                        |
| Mittlere Zeit bis zur Hämostase                                                                                             | 1,2 Minuten  | 1,6 Minuten <sup>a</sup>  |
| Mittlere Zeit bis zur Mobilisierung                                                                                         | 72,2 Minuten | 87,5 Minuten <sup>b</sup> |
| Inzidenz schwerer vaskulärer Komplikationen <sup>c</sup>                                                                    | 0 (0 %)      | 1 (2 %)                   |
| Anzahl der Patienten mit unerwünschten Ereignissen                                                                          | 5 (25 %)     | 19 (32 %)                 |
| Behandlungsversagen (definiert als schwere vaskuläre Komplikationen, Notwendigkeit einer manuellen Kompression oder beides) | 0 (0 %)      | 3 (5 %)                   |
| Fehlfunktionen des Produkts                                                                                                 | 0 (0 %)      | 6 (10 %)                  |

<sup>a</sup>Basierend auf einer Gesamtstichprobengröße von 58, da 2 Patienten zum Zeitpunkt des Eingriffs aufgrund vorheriger ipsilateraler Punktionen keine Hämostase erreichten. Die Hämostase wurde bei diesen Patienten nach 7 Minuten bzw. nach 37 Minuten erreicht.

<sup>b</sup>Basierend auf einer Gesamtstichprobengröße von insgesamt 59: 1 Patient wurde nicht berücksichtigt, weil er aufgrund eines Lungenödems an ein Beatmungsgerät angeschlossen wurde und über eine Woche lang nicht mobil war.

<sup>c</sup>Definiert als vaskuläre Komplikation, die eine Bluttransfusion oder eine operative Intervention erfordert, oder lokale Infektion, die die Verabreichung von Antibiotika, einen Krankenhausaufenthalt oder eine Verlängerung des Krankenhausaufenthalts oder ein Debridement der betroffenen Stelle erfordert.

In Abschnitt 1 der Studie wurden keine größeren vaskulären Komplikationen beobachtet. In Abschnitt 2 der Studie wurde eine schwere vaskuläre Komplikation verzeichnet: ein Pseudoaneurysma, das innerhalb eines Tages nach dem Eingriff auftrat. Das Ereignis erforderte eine ultraschallgeführte Kompression und eine Thrombininjektion in das Pseudoaneurysma und verlängerte den Krankenhausaufenthalt des Patienten.

Von den fünf unerwünschten Ereignissen, die in Abschnitt 1 der Studie berichtet wurden, gab es ein möglicherweise produktbedingtes unerwünschtes Ereignis: ein nicht schwerwiegendes Ereignis mit starken Blutungen am ersten Tag nach dem Eingriff. Von den 19 unerwünschten Ereignissen, die in Abschnitt 2 der Studie berichtet wurden, wurden drei produktbedingte, nicht schwerwiegende unerwünschte Ereignisse in Form von Hämatomen und sechs möglicherweise produktbedingte, nicht schwerwiegende Ereignisse beobachtet, darunter drei Berichte über anhaltende Sickerblutungen, zwei Hämatome und ein Beinschmerz nach Belastung.

In Abschnitt 2 gab es drei Patienten, bei denen die Behandlung fehlschlug: Bei zweien war dies darauf zurückzuführen, dass die Hämostase ohne Kompression nicht erreicht werden konnte, und bei einem darauf, dass es zu einer schweren vaskulären Komplikation (Pseudoaneurysma) kam. In Abschnitt 1 der Studie kam es zu keinem Behandlungsversagen.

Von den sechs Fehlfunktionen des Produkts in Abschnitt 2 der Studie beeinträchtigten drei das Verfahren nicht, eine wurde auf einen Anwenderfehler zurückgeführt, eine war eine Undichtigkeit der Einführschleuse und eine war eine gebrochene Filamentverbindung. Die beiden letztgenannten Probleme wurden durch Aktualisierungen bei der Version Nr. C11202 gelöst.

In Abschnitt 2 der klinischen Studie vor dem Inverkehrbringen wurden die Ergebnisse der 6-monatigen Nachbeobachtung aufgrund der Nichteinhaltung der Vorgaben durch die Patienten nicht berichtet. Die 30-Tage-Ergebnisse der klinischen Studie vor dem Inverkehrbringen (EU-SE-001), die mit dem in der klinischen Literatur angegebenen Nachbeobachtungszeitraum übereinstimmen, zeigen, dass das FemoSeal™ VCS sicher und wirksam ist.

#### 1.4.2 Zusammenfassung der Daten aus klinischen Studien nach dem Inverkehrbringen

Es gibt vier abgeschlossene klinische Studien nach dem Inverkehrbringen, die in der folgenden **Tabelle 1.6** beschrieben sind. Diese klinischen Studien sind weder veröffentlicht noch online verfügbar.

**Tabelle 1.6 Klinische Studien nach dem Inverkehrbringen**

| Klinische Studien nach dem Inverkehrbringen                                                 |              |                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                     |
|---------------------------------------------------------------------------------------------|--------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|
| Name der Studie                                                                             | Jahr/CI      | Art der Studie                                                           | Ziele                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Meilensteine                                                                                                                                                                                                                                                                                                                                                                              | Mögliche Akzeptanzkriterien                                                                                                                         |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI | Studie nach dem Inverkehrbringen, Benutzerakzeptanz der neuen Verpackung | Studie nach dem Inverkehrbringen, zur Dokumentation der Funktionalität, durchgeführt mit dem aktualisierten FemoSeal Vascular® Closure System Nr. 11202, das im Vergleich zur ersten Version Nr. 11200 über ein modifiziertes Applikationssystem verfügt.<br><br>Ziel der Studie war es, Rückmeldungen zur überarbeiteten Bedienungsanleitung (Instructions for Use, IFU) und zum Schulungsprojekt für Ärzte und Pflegepersonal zu erhalten, die in der Risikoanalyse vorgenommenen | 100 Patienten <ul style="list-style-type: none"> <li>63 männlich/37 weiblich</li> <li>Durchschnittsalter der Frauen betrug 68 Jahre und das der Männer 65 Jahre</li> </ul> 2 Krankenhäuser in Schweden, 6 Ärztinnen und Ärzte<br><br>112 Produkte<br><br>In Patientenakten (Case Report Forms, CRF) erfasste Daten<br><br>Geplante Beobachtungszeit – 30 Minuten ab Applikationszeitpunkt | Ergebnisse<br><br>1. Abbildungen/Anweisungen in der Bedienungsanleitung gelten als informativ und angemessen<br><br>2. Sofortige Hämostase (91/100) |

|                                                                                   |                                                                  |                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|-----------------------------------------------------------------------------------|------------------------------------------------------------------|--------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|----|-----|----------|-------|----------|-----------|----|-----------|-----------|-------------------------|----------|--------------------|------------|---------------------|-----------|-------------------|---------|-----------------------|----------|--------------------------------|----------|----------------------|-----------|--------------------------|-----------|-----------------------------------|----------|----------------------|--------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                   |                                                                  |                                                  | Bewertungen zu bestätigen und Anregungen für eventuelle Verbesserungen der Produktqualität zu geben.                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008) | Dr. Nicolas Moes, Medizinische Universität Innsbruck, Österreich | Bestätigende Bewertung nach dem Inverkehrbringen | Ziel dieser Studie war es, die Sicherheit und Leistungsfähigkeit von FemoSeal® bei der Verwendung in der normalen klinischen Routine bei Patienten zu bewerten, die sich einer diagnostischen Herzkatheteruntersuchung oder einem perkutanen kardiologischen Eingriff mit einer 7F-Schleuse unterziehen. | 50 konsekutive Patienten<br><br>Indikation: diagnostische oder invasive Herzkatheterisierung über die A. femoralis communis<br><br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Primäre Endpunkte <ul style="list-style-type: none"><li>Primärer Wirksamkeitsendpunkt – TTH (Zeit bis zur Hämostase) mit oder ohne Sickerblutung, aber ohne zusätzliche manuelle oder mechanische Kompression.</li><li>Sicherheitsendpunkt – Inzidenz unerwünschter Ereignisse – kleinere und größere vaskuläre Komplikationen und alle anderen unerwünschten Ereignisse – schwerwiegende und nicht schwerwiegende – während der Dauer der Studie (d. h. bis zur Entlassung des Patienten).</li></ul> Ergebnisse <ul style="list-style-type: none"><li>Mittlere Zeit bis zur Hämostase</li><li>Diagnostisch – 56,6 ± 29 Sekunden</li><li>Interventionell – 59,9 ± 16,2 Sekunden</li><li>Alle Patienten 57,8 ± 26,3</li><li>Alle Patienten konnten nach 4 Stunden Bettruhe problemlos mobilisiert werden.</li></ul> Sicherheitsergebnisse <ul style="list-style-type: none"><li>49/50 (98 %) frei von vaskulären Komplikationen bis zur Entlassung aus dem Krankenhaus</li><li>Mittlere Zeit bis zur Entlassung: 2,6 Tage</li><li>1/50 (2 %) leichte Blutungen am nächsten Tag nach ereignisloser Mobilisation am Tag der Angiographie</li></ul> |
| n                                                                                 | 50                                                               |                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| men                                                                               | 35 (70%)                                                         |                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| women                                                                             | 15 (30%)                                                         |                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| PCI cases                                                                         | 15                                                               |                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| age (yrs)                                                                         | 62.8±11.1                                                        |                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| body mass index (kg/m²)                                                           | 25.4±6.7                                                         |                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| systolic BP (mmHg)                                                                | 131.2±20.9                                                       |                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| diastolic BP (mmHg)                                                               | 77.9±10.6                                                        |                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| diabetes mellitus                                                                 | 9 (18%)                                                          |                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| arterial hypertension                                                             | 34 (68%)                                                         |                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| previous coronary intervention                                                    | 13 (26%)                                                         |                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| preprocedure aspirin                                                              | 50 (100%)                                                        |                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| preprocedure clopidogrel                                                          | 50 (100%)                                                        |                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Procedural unfractionated heparin                                                 | 15 (30%)                                                         |                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Procedural abciximab                                                              | 2 (4%)                                                           |                                                  |                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |

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| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | 2009 RADI                       | Studie nach dem Inverkehrbringen                                          | <p>Die Studie sollte Aufschluss darüber geben, ob die Kunden/Verwender Probleme mit der neuen Verpackung wahrgenommen haben, insbesondere mit der nicht sterilen Außenseite des Tuvek/PET-PE-Beutels.</p> <p>Die Studie sollte auch Aufschluss darüber geben, ob der behandelnde Arzt Unterschiede bei den Anwendungs-/Einsetzschritten des Produkts im Vergleich zu früher verwendeten Produkten wahrnimmt.</p> <p>Die Studie sollte auch Hinweise auf weitere Erfordernisse zur Verbesserung der Produktqualität liefern.</p> | <p>25 Produkte</p> <p>4 Krankenhäuser in Schweden</p> <p>16/25 (64 %) der Patienten waren PCI-Patienten mit schweren Antikoagulationsmedikamenten</p>                                                                                                                                                                                                                                                                                                                                              | <p>Ergebnisse</p> <ol style="list-style-type: none"> <li>Probleme im Zusammenhang mit der Verpackung – 21/25 (84 %) der Implantationen waren erfolgreich; 4/25 (16 %) waren nicht erfolgreich (1 – Testen der neuen Einführschleuse, 1 Innenscheibe bei der Arteriotomie während der Rückwärtsbewegung, Taste wurde nach oben gedrückt, und die äußere Sperrscheibe wurde in den Inzisionskanal platziert, 2 sofortige Hämostase wurde nicht erreicht, obwohl es keine Probleme beim Einsetzen gab.)</li> <li>Sofortige Hämostase: 19/25 (76 %) Patienten</li> <li>Blutungen: 11/25 (44 %) – 9/25 (36 %) Sickerblutungen/Blutungen, 2/25 (8 %) Hämatome</li> </ol> <p>Ereignisrate gesamt: 19 %</p>                                            |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022) | 2022/Terumo Medical Corporation | Prospektive, multizentrische Beobachtungsstudie nach dem Inverkehrbringen | <p>Zur weiteren Demonstration der Sicherheit und Wirksamkeit des FemoSeal™ VCS bei der Erzielung der Hämostase von Zugangsstellen zur A. femoralis communis (CFA) bei Patienten, die sich perkutanen endovaskulären Eingriffen unterziehen.</p>                                                                                                                                                                                                                                                                                 | <ul style="list-style-type: none"> <li>Nachbeobachtung des Patienten nach 30 Tagen (<math>\pm</math> 7 Tage) im Rahmen eines Krankenhaustermens oder Telefonanrufs.</li> <li>Aufnahme in die Studie: Dezember 2021 bis Juli 2022.</li> <li>Bei 230 aufgenommenen Teilnehmern werden diagnostische oder interventionelle endovaskuläre Eingriffe mit dem FemoSeal™ durchgeführt</li> </ul> <p>3 Orte in Europa: Frankreich (92 Patienten), Deutschland (38 Patienten), Belgien (100 Patienten).</p> | <ul style="list-style-type: none"> <li><b>Demografie/ Komorbiditäten:</b> <ul style="list-style-type: none"> <li>- Geschlecht: 161 Männer (70 %)/69 Frauen (30 %).</li> <li>- Durchschnittsalter: 70 <math>\pm</math> 12.</li> <li>- BMI: 26,1 <math>\pm</math> 4,95 kg/m<sup>2</sup>.</li> <li>- Hypertonie: 160 Patienten (69,6 %).</li> <li>- Dyslipidämie: 128 (55,7 %).</li> <li>- Koronargefäßerkrankung: 42 (18,3 %).</li> <li>- Raucher: 86 (37,6 %).</li> <li>- Ex-Raucher: 66 (28,8 %).</li> <li>- Koronare Herzkrankheit: 34 (14 %).</li> <li>- Myokardinfarkt in der Anamnese: 18 (7,8 %).</li> <li>- Nebengefäß-Revaskularisierung: 12 (5,2 %) Karotis und 83 (37,5 %) und Arterie der unteren Gliedmaßen.</li> </ul> </li> </ul> |

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|  |  |  |  |  | <ul style="list-style-type: none"> <li>- Antithrombozytäre Therapie (zu Studienbeginn): 211 (91,7 %), einschließlich dualer antithrombozytärer Therapie (DAPT): 21 (9,1 %).</li> <li>- Orale Antikoagulation: 40 (17,4 %) Patienten.</li> <li>• <b>Interventionsmerkmale:</b> <ul style="list-style-type: none"> <li>- Umstände: stationäre Klinik 162 Fälle (70,4 %), ambulante Klinik 68 Fälle (29,6 %).</li> <li>- Vorrangige Indikation: Claudicatio 147 Fälle (63,9 %).</li> <li>- Ansatz: 35 antegrad (15,3 %), 194 retrograd (84,7 %).</li> </ul> </li> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Kombiniertes Endpunkt Sicherheit (keine größeren Komplikationen an der Extremität mit der Zugangsstelle innerhalb von 6 Stunden nach dem Eingriff) und Wirksamkeit (erfolgreiche Hämostase an der Punktionsstelle) erreicht bei 215/226 (95,1 %) [95 % KI: 91,46; 97,55] Patienten in der Gesamtgruppe und 215/230 (93,5 %) [95 % KI 89,47, 96,30] in der mit FemoSeal™ behandelten Gruppe.</li> <li>- Der Wirksamkeitsendpunkt wurde bei 219/226 (96,9 %) KI [93,7, 98,7] Patienten erreicht.</li> <li>- Der Sicherheitsendpunkt wurde bei 220/230 (95,2 %) [95 % KI: 92,15, 97,90] Patienten erreicht.</li> </ul> </li> <li>• <b>Sekundäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Der Endpunkt „keine kleineren</li> </ul> </li> </ul> |
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|  |  |  |  | <p>Komplikationen an der Zugangsstelle innerhalb von sechs Stunden nach dem Eingriff“ wurde bei 225/230 (97,8 %) [95 %-KI: 95,00; 99,29] Patienten erreicht.</p> <p>- Der Endpunkt „keine kleineren oder großen Komplikationen an der Zugangsstelle im Zeitraum von sechs Stunden bis 30 Tage nach dem Eingriff“ wurde bei 219/230 (95,2 %) [95 % KI: 91,60; 97,59] Patienten erreicht.</p> <p>- Mediane Zeit bis zur Hämostase mit FemoSeal™ VCD: 0,42 (0,25; 0,50) Minuten.</p> <p>- Mediane Zeit bis zur Mobilisierung 5,00 (4,54; 5,50) Minuten.</p> <p>- Mediane Dauer des Krankenhausaufenthalts: 23,98 (22,72; 25,00) Stunden.</p> <p>- Gebrauchstauglichkeit des FemoSeal™ VCS: „einfache“ oder „sehr einfache“ Platzierung in 98,7 % der Fälle („einfache“ Platzierung bei 21 (9,2 %), „sehr einfache“ Platzierung bei 205 (89,5 %)) ohne oder bei geringem Widerstand während der Platzierung in 226 Fällen (98,3 %).</p> <p>152/230 (66,1 %) der Patienten wurden mit dem im FemoSeal™ Kit enthaltenen und für FemoSeal™ empfohlenen Führungsdraht (GW 0,038") behandelt, ohne dass Produktfehler oder unerwünschte Ereignisse gemeldet wurden.</p> |
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Die Studie aus dem Jahr 2006 wurde durchgeführt, um die Sicherheit und Wirksamkeit des aktuellen Produkts mit einem verbesserten Applikationssystem zu bestätigen und um Rückmeldungen zur Bedienungsanleitung des FemoSeal™ VCS und zum Schulungsprogramm zu erhalten. Die Studie umfasste 100 Patienten, und der primäre Endpunkt war, ob eine Hämostase erreicht wurde oder ob zusätzliche manuelle oder mechanische Maßnahmen zur Kompression erforderlich waren. Diese Studie kam zu dem Schluss, dass die Anwendung von FemoSeal™ VCS in den meisten Fällen erfolgreich war (sofortige Hämostase in 91 % der Fälle).

In die Studie aus dem Jahr 2008 wurden 50 Patienten aufgenommen, um die Sicherheit und Leistungsfähigkeit des FemoSeal™ VCS bei der Anwendung in der normalen klinischen Routine bei Patienten zu bewerten, die sich einer Herzkatheteruntersuchung mit einer 7Fr-Schleuse unterziehen. Der primäre Endpunkt der Studie war die Erhebung von Daten über die Zeit bis zur Hämostase und die Zeit bis zur Mobilisierung ohne zusätzliche manuelle oder mechanische Kompression. Die Studienergebnisse zeigten, dass die durchschnittliche Zeit bis zur Hämostase 57,8 Sekunden betrug und alle Patienten nach 4 Stunden Bettruhe mobilisiert werden konnten.

Die Studie aus dem Jahr 2009 sollte die neue Verpackung des FemoSeal™ VCS evaluieren. Dazu wurden 25 Patienten in die Studie aufgenommen. Der primäre Endpunkt war, ob der Benutzer Probleme mit der Verpackung hatte. Die Benutzer stellten keine Probleme mit der neuen Verpackung des FemoSeal™ VCS fest. In dieser Studie wurden auch Daten für die Zeit bis zur Hämostase erhoben.

Im Rahmen der Studie im Jahr 2022 sollten Daten zur Sicherheit und Wirksamkeit des FemoSeal VCS bei der Erzielung der Hämostase von Zugangsstellen zur A. femoralis communis (CFA) bei Patienten, die sich perkutanen endovaskulären Eingriffen unterziehen, proaktiv erfasst werden. Dazu wurden 230 Patienten in die Studie aufgenommen. Die primären Endpunkte für das Register sind der Erfolg des Eingriffs (d. h. erfolgreiche Hämostase an der Punktionsstelle) und die Reduzierung schwerwiegender Komplikationen (z. B. Gefäßverletzungen, Blutungen an der Zugangsstelle, Infektionen an der Zugangsstelle, wiederholte manuelle Kompression und neue ipsilaterale akute Beinischämie an der Zugangsstelle). Die Schlussfolgerung aus der Studie war, dass das FemoSeal™ VCS in der Praxis gut funktioniert und eine effektive Hämostase sowie niedrige Raten von Komplikationen an der Zugangsstelle für Patienten ermöglicht, die sich peripheren endovaskulären Eingriffen unterziehen. Es konnte eine gute Leistung mit kurzer Zeit bis zur Hämostase festgestellt werden, und die Rückmeldungen der Benutzer zur Gebrauchstauglichkeit waren positiv, was FemoSeal™ VCS zu einem wertvollen Produkt zum Verschluss des femoralen Zugangs macht.

### 1.4.3 Zusammenfassung der Daten aus klinischen Nachbeobachtungsstudien nach dem Inverkehrbringen

#### 1.4.3.1 Abgeschlossene Aktivitäten der klinischen Nachbeobachtung nach dem Inverkehrbringen

Eine Zusammenfassung der abgeschlossenen klinischen Nachbeobachtungen nach dem Inverkehrbringen ist in **Tabelle 1.7** unten beschrieben.

**Tabelle 1.7. Klinische Nachbeobachtungen nach dem Inverkehrbringen**

| Abgeschlossene klinische Nachbeobachtungsaktivitäten nach dem Inverkehrbringen |             |                                                                              |                                                                                                                                                                                                          |                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|--------------------------------------------------------------------------------|-------------|------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Bezeichnung der Aktivität                                                      | Jahr/ KI    | Art der Studie                                                               | Ziele                                                                                                                                                                                                    | Meilensteine                                                                                                                                                                                             | Mögliche Akzeptanzkriterien                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021)      | 2021<br>TMC | Klinische Studie nach dem Inverkehrbringen – hochwertige Umfrage             | Umfrage nach dem Inverkehrbringen, um prospektives Feedback im Zusammenhang mit der Verwendung des FemoSeal™ Gefäßverschlussystems zu sammeln, das auf dem Markt der Europäischen Union vertrieben wird. | <ul style="list-style-type: none"> <li>• 120 Fälle</li> <li>• 8 verschiedene Ärztinnen und Ärzte mit &gt; 5 Jahren Erfahrung</li> <li>• Mehrere Länder in Europa</li> </ul>                              | <b>Produktbewertungen auf einer Skala von 1 bis 5 – Aussagen in der Umfrage</b> <ul style="list-style-type: none"> <li>• Akzeptanzkriterien <ul style="list-style-type: none"> <li>○ Ratings von 3 bis 5 gelten als günstig</li> <li>○ Alle Aussagen sollten ≥ 80 % positives Feedback haben</li> </ul> </li> <li>• Ergebnisse <ul style="list-style-type: none"> <li>○ Keine Aussage in der Umfrage erhielt &gt; 20 % ungünstige Antworten</li> <li>○ Keine Beschwerden hinsichtlich des Produkts eingetragen</li> </ul> </li> </ul> |
| 20210298 – 0,035” and 0038” Guidewire Clinical Survey Report (2021)            | 2021<br>TMC | Klinische Umfrage nach dem Inverkehrbringen – qualitativ hochwertige Umfrage | Umfrage nach dem Inverkehrbringen, um prospektives Feedback im Zusammenhang mit der Verwendung des 0,035"-Führungsdrahts zu sammeln, der im Lieferumfang des 6-Fr-Angio-Seal™ VIP                        | <ul style="list-style-type: none"> <li>• Umfragen für 0,035"-Draht <ul style="list-style-type: none"> <li>○ 106 Umfragen</li> <li>○ 64 Ärzte</li> </ul> </li> <li>• Umfragen für 0,038"-Draht</li> </ul> | <b>Produktbewertungen auf einer Skala von 1 bis 5 – Aussagen in der Umfrage</b> <ul style="list-style-type: none"> <li>• Akzeptanzkriterien <ul style="list-style-type: none"> <li>○ Ratings von 3 bis 5 gelten als günstig</li> <li>○ Alle Aussagen sollten ≥ 80 %</li> </ul> </li> </ul>                                                                                                                                                                                                                                            |

| Abgeschlossene klinische Nachbeobachtungsaktivitäten nach dem Inverkehrbringen                                                  |                         |                                                                  |                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|---------------------------------------------------------------------------------------------------------------------------------|-------------------------|------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                 |                         |                                                                  | Vascular Closure Systems (VCD) enthalten ist, und des 0,038"-Führungsdrahts, der sowohl im Lieferumfang des 8-Fr-Angio-Seal™ VIP VCD als auch des FemoSeal Vascular Closure Systems enthalten ist, die in der Europäischen Union vertrieben werden. | <ul style="list-style-type: none"> <li>○ 109 Umfragen</li> <li>○ 55 Ärzte</li> <li>• 12 retrospektive Umfragen</li> </ul>                                                                                                                                                                                                                                                                 | <ul style="list-style-type: none"> <li>positives Feedback haben</li> <li>• Ergebnisse <ul style="list-style-type: none"> <li>○ Alle Führungsdrähte wurden als akzeptabel eingestuft</li> <li>○ Keine Beschwerden hinsichtlich des Produkts eingetragen</li> </ul> </li> </ul>                                                                                                                                                                                                                                                                                                                                                  |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023–2024<br><br>TMC/TE | Klinische Studie nach dem Inverkehrbringen – hochwertige Umfrage | Prospektives Sammeln von Feedback im Zusammenhang mit der Verwendung des FemoSeal VCS mit Führungsdrähten, die auf dem EU-Markt vertrieben werden.                                                                                                  | <ul style="list-style-type: none"> <li>• 126 Umfragen <ul style="list-style-type: none"> <li>• 7 Orte</li> <li>• 5 Länder</li> </ul> </li> <li>• 14. November 2023 – 11. Juni 2024</li> <li>• Medizinisches Fachgebiet des Arztes/der Ärztin: <ul style="list-style-type: none"> <li>○ Gefäßchirurgie</li> <li>○ Interventionelle Radiologie</li> <li>○ Angiologie</li> </ul> </li> </ul> | <b>Produktbewertungen auf einer Skala bis 5 – Aussagen in der Umfrage</b> <ul style="list-style-type: none"> <li>• Akzeptanzkriterien <ul style="list-style-type: none"> <li>○ Ratings von 3 bis 5 gelten als günstig</li> <li>○ Alle Aussagen sollten ≥ 80 % positives Feedback haben</li> <li>○ Falls unerwünschte Ereignisse in dieser Umfrage zutage treten, sollten es diejenigen sein, die im Rahmen des Risikomanagements erwartet werden.</li> </ul> </li> <li>• Patientendatendemografie <ul style="list-style-type: none"> <li>○ Frauen: 29,4 % (37/126)</li> <li>○ Männlich: 69,8 % (88/126)</li> </ul> </li> </ul> |

| Abgeschlossene klinische Nachbeobachtungsaktivitäten nach dem Inverkehrbringen |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|--------------------------------------------------------------------------------|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                |  |  |  |  | <ul style="list-style-type: none"> <li>○ Geschlecht nicht angegeben: 0,8 (1/126)</li> <li>○ Alter &gt; 75 Jahre: 31,7 %</li> <li>• Ergebnisse <ul style="list-style-type: none"> <li>○ Im Lieferumfang des FemoSeal™ VCS enthaltener Führungsdraht: 101/126 (80,2 %).</li> <li>○ Verfahrensdauer (Minuten): 63,4 (36,6) (Mittelwert (SD)); 57,0 (36,0–81,0) (Median (IQR))</li> <li>○ Alle Leistungsbewertungen des FemoSeal™ VCS waren positiv.</li> <li>○ Alle mit dem FemoSeal™ VCS gelieferten Führungsdrähte wurden positiv bewertet.</li> <li>○ Ein unerwünschtes Ereignis (0,8 %): Die FemoSeal™ VCS Scheiben waren nicht gut ausgerichtet, vermutlich, weil ein steifer Führungsdraht</li> </ul> </li> </ul> |

| Abgeschlossene klinische Nachbeobachtungsaktivitäten nach dem Inverkehrbringen |  |  |  |  |                                                                                                                                                 |
|--------------------------------------------------------------------------------|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                |  |  |  |  | (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 Zoll) verwendet wurde, der manuelle Kompression erfordert, um eine Hämostase zu erreichen. |

Die Terumo Medical Corporation hat im laufenden Berichtszeitraum (01. September 2019 – 31. August 2024) drei hochwertige Umfragen unter Ärzten durchgeführt.

In den klinischen FemoSeal™ Umfragen wurden proaktiv klinische Daten in Bezug auf die Sicherheit und Leistung des FemoSeal™ VCS während der klinischen Verwendung erhoben. Die Umfrage umfasste Fragen zum gesamten Produkt und zu seinem Zubehör, einschließlich des 0,038-Zoll-Führungsdrahts, sowie zu deren direkter Interaktion. In den klinischen Umfragen zum Führungsdraht wurden proaktiv klinische Daten in Bezug auf Sicherheit und Leistung während der klinischen Verwendung des 0,038-Zoll-Führungsdrahts erfasst, der mit dem FemoSeal™ VCS geliefert wird. Die Fragen konzentrierten sich speziell auf die allgemeine Verwendung des Führungsdrahtes, von der Einführung durch die Prozedurschleuse in das Gefäßsystem bis zur Entfernung des Drahts.

Das FemoSeal™ VCS und der 0,038-Zoll-Führungsdraht, der dem Produkt beiliegt, erhielten beide akzeptable Bewertungen. Basierend auf der Auswertung der Kommentare aus den hochwertigen klinischen Umfragen wurden sechs (6) Reklamationen des Produkts und neun (9) Nichtbeanstandungen des Führungsdrahts eingereicht. Die Reklamationen wurden sowohl für FemoSeal als auch für den Führungsdraht ausgewertet und im Rahmen der Überwachung nach dem Inverkehrbringen durch Terumo beurteilt. Es wurden keine neuen Risiken und/oder Risikostufen identifiziert.

Im Rahmen der PMCF-Aktivitäten wurde 2024 eine Umfrage bei Ärzten durchgeführt. Die Ergebnisse der Umfrage zeigten, dass die Leistungsbewertung und Sicherheit des FemoSeal™ VCS insgesamt sehr positiv ausfielen. Die Kompatibilität anderer Führungsdrähte als des standardmäßig mit dem FemoSeal™ VCS gelieferten wurde ebenfalls nachgewiesen.

#### 1.4.3.2 Laufende/geplante klinische Nachbeobachtung nach dem Inverkehrbringen

TMC hat eine laufende/geplante klinische Nachbeobachtungsstudie nach dem Inverkehrbringen. Eine klinische Umfrage wird durchgeführt, um prospektiv Rückmeldungen in Bezug auf die Verwendung des Führungsdrahts mit FemoSeal VCS zu erfassen, der auf dem EU-Markt vertrieben wird. Die Umfrage wird von den Ärzten ausgefüllt, um zu untersuchen, welche Führungsdrähte sie während des Eingriffs verwendet haben. Fehlende Literatur und Kommentare externer Prüfer zur Kompatibilität des FemoSeal™ VCS mit der Verwendung anderer Führungsdrähte von Nicht-Terumo-Marken wurde als Lücke identifiziert, die mit dieser Umfrage geschlossen werden soll. Die Rückmeldungen beziehen sich unter anderem auf technische Ergebnisse und auf die klinische Leistung und Sicherheit bei der Verwendung des Produkts mit verschiedenen Führungsdrähten.

#### 1.4.4 Zusammenfassung der Daten aus der systematischen Literaturrecherche

Die Terumo Medical Corporation führt systematische Literaturrecherchen durch, um klinische Sicherheits- und Leistungsdaten aus veröffentlichten Studien zum FemoSeal™ VCS und/oder ähnlichen Produkten zu erfassen und zu bewerten. Ziel der jährlichen Prüfung der veröffentlichten Literatur ist es, zuvor unbekannte Nebenwirkungen zu ermitteln, bekannte Nebenwirkungen zu überwachen, entstehende Risiken zu ermitteln und eine mögliche systematische fehlerhafte oder zulassungsüberschreitende Verwendung des FemoSeal™ VCS festzustellen.

Bei der jüngsten systematischen Literaturrecherche, die den Zeitraum vom 1. September 2019 bis zum 31. August 2024 abdeckt, wurden 29 veröffentlichte Studien ermittelt, die klinische Daten zur Sicherheit und Leistung des FemoSeal™ VCS lieferten. In dreiundzwanzig Referenzen wurde ein On-Label-Gebrauch des FemoSeal™ VCS aufgeführt, in neun Studien ein Off-Label-Gebrauch gemeldet. Insgesamt zeigt die Literaturlauswertung über Studien, die sich speziell mit der Verwendung des FemoSeal™ VCS befassen, dass die untersuchte Population repräsentativ für Patienten in der EU ist, die sich perkutanen Gefäßkathetereingriffen unterziehen. Eine Liste dieser 23 nach dem Peer-Review-Verfahren überprüften On-Label-Anwendungen finden Sie in **Abschnitt 3**.

Die klinische Leistung wurde anhand der folgenden Kriterien bewertet:

- Die Zeit bis zur Hämostase ist besser als oder vergleichbar mit dem Stand der Technik für den perkutanen Verschluss der A. femoralis communis.
- Die Zeit bis zur Mobilisierung ist besser als oder vergleichbar mit dem Stand der Technik für den perkutanen Verschluss der A. femoralis communis.
- Die Rate postoperativer Komplikationen ist im Vergleich zum aktuellen Versorgungsstandard ähnlich hoch oder niedriger.

Auf der Grundlage dieser klinischen Leistungsdaten haben die Daten dieser Literaturlauswertung gezeigt, dass das FemoSeal™ VCS erfolgreich zum Verschließen der femoralen Arterienpunktion

(Arteriotomie) bei Patienten eingesetzt werden kann, die sich einer perkutanen Katheterisierung unter Verwendung einer 7Fr-Prozedurschleuse (oder kleiner) unterzogen haben. Die vollständige Hämostase wurde bei der Mehrheit der Patienten (79,65–100 %) erreicht und war mit einer medianen Zeit bis zur Hämostase von 0,5 Minuten und einer mittleren Zeit bis zur Entlassung von 3 Tagen verbunden. Zwischen 69,2 und 86,7 % der Patienten konnten 5 Stunden nach dem Verschluss umherlaufen, bei einer mittleren postoperativen Liegezeit von 349 Minuten. Ein Versagen des FemoSeal™ VCS wurde in 3,68–4 % der Fälle beobachtet, und bei 0,9–4,4 % der Eingriffe war zusätzliche manuelle Kompression erforderlich.

Die klinische Sicherheit wurde anhand unerwünschter Ereignisse bewertet, einschließlich, aber nicht beschränkt auf:

- Blutung
- Hämatom
- Pseudoaneurysma
- Hämatom
- Arteriovenöse Fistel
- Infektion
- Tod

Im Hinblick auf jedes dieser unerwünschten Ereignisse war die Häufigkeit des Auftretens bei FemoSeal™ VCS in den eingeschlossenen Studien geringer oder vergleichbar mit den in der Vergangenheit berichteten Raten für manuelle Kompression und andere Gefäßverschlussprodukte.

Bei der Überprüfung von zehn Fallberichten wurden keine unerwünschten Ereignisse festgestellt, da keine neuen, unerwarteten, neu auftretenden oder unannehmbaren Risiken identifiziert wurden.

Die Gesamtwirksamkeit der Verwendung des FemoSeal™ VCS während einer diagnostischen Angiographie oder interventionellen Operation hängt von mehreren Faktoren ab, wie z. B. Geschlecht, Alter, Anatomie des Patienten, Begleiterkrankungen, anatomische Platzierung der Punktionsstelle, Erfahrung des Chirurgen, VCD-Platzierungsmethode, postoperative Versorgung, usw. Neben dem Verschlusserfolg, einschließlich des Erreichens der Hämostase, bot FemoSeal™ VCS klinische Vorteile im Vergleich zum Gefäßverschluss nach der Punktierung der Oberschenkelarterie, wie z. B. verkürzte Zeit bis zur Hämostase und verkürzte Zeit bis zur Mobilisierung. Die Ergebnisse in Bezug auf die Leistung des FemoSeal™ VCS entsprechen denen, die bei bestimmungsgemäßer Verwendung für diesen Produkttyp zu erwarten sind. Einige der während des aktuellen Suchzeitraums abgerufenen Referenzen zeigten die Verwendung des Prüfprodukts an einer anderen anatomischen Stelle als der A. femoralis communis und zum Verschluss von Arteriotomien > 7 Fr, was als Off-Label gilt.



Während der Überprüfung wurden keine unbekannten Nebenwirkungen, neu auftretenden Risiken oder mögliche systematische fehlerhafte Verwendungen des Produkts festgestellt. Wenn das FemoSeal™ VCS jedoch von geschulten Ärzten mit Sorgfalt verwendet wird, funktioniert das Medizinprodukt als nützliches und notwendiges klinisches Gerät. Insgesamt erfüllt die Zieltherapie und damit das FemoSeal™ VCS den derzeit bestehenden klinischen Bedarf bei der Behandlung von Komplikationen im Zusammenhang mit dem Gefäßzugang.

Insgesamt ergaben die Daten dieser Literaturlauswertung keine bisher unbekannten Leistungs- oder Sicherheitsprobleme im klinischen Umfeld oder unerwünschte Wirkungen, die häufiger als erwartet/akzeptabel auftraten. Daher kann aus dieser Literaturlauswertung geschlossen werden, dass das FemoSeal™ VCS, wenn es zur Kompression für die Hämostase an der Arteriotomie nach perkutaner Katheterisierung verwendet wird, weiterhin die erwartete Leistung erbringt und nicht mit schwerwiegenden Sicherheitsereignissen verbunden ist.

#### **1.4.5 Zusammenfassung der Daten aus der Überwachung nach dem Inverkehrbringen**

Ein proaktives System zur Überwachung nach dem Inverkehrbringen ist vorhanden, und eine Prüfung aller Beschwerden wird monatlich und in Übereinstimmung mit den internen Herstellungsverfahren durchgeführt. Die Beschwerdendaten wurden im Zeitraum vom 1. September 2019 bis zum 31. August 2024 analysiert. Insgesamt wurden 28 MDV-Berichte (Medical Device Vigilance) und 476 Kundenreklamationen an den Hersteller übermittelt. Von den 28 MDV-Meldungen betrafen 27 unerwünschte Ereignisse und eine eine Fehlfunktion des Produkts. Während des Berichtszeitraums gab es zwei Todesfälle, aber keiner der gemeldeten Todesfälle wurde als mit dem Prüfprodukt zusammenhängend beurteilt. Von den 476 Reklamationen an den Hersteller waren die häufigsten Reklamationsgründe Probleme beim Platzieren (146 Vorkommnisse, 0,0142 % Häufigkeitsrate). „Fehlermöglichkeiten beim Herausziehen“ wird mit einer Rate von 0,0126 % (130 Ereignisse) am zweithäufigsten genannt.

Das FemoSeal™ Vascular Closure System wurde weltweit über 1.030.136 Mal und im europäischen Wirtschaftsraum über 827.843 Mal verkauft. Die berechnete Häufigkeit von Reklamationen auf Grundlage des Gesamtumsatzes beträgt 0,046 %. Insgesamt ist die Reklamationsquote durch Kunden sehr gering. Es wurden keine neuen Risiken identifiziert, die nicht in der Bedienungsanleitung und Risikodokumentation enthalten sind.

Die Häufigkeit des Auftretens der unerwünschten Nebenwirkungen ist in **Tabelle 1.2** dargestellt. Es wurden keine neuen unerwarteten, neu entstehenden oder unververtretbaren Risiken durch diese Reklamationen identifiziert. Es gab keinen signifikanten Anstieg der Häufigkeit oder des Schweregrads bekannter unerwünschter Nebenwirkungen.



#### 1.4.6 Allgemeine Zusammenfassung der klinischen Leistung und Sicherheit

FemoSeal™ VCS ist für den Einsatz beim Verschluss der A. femoralis communis (Arteriotomie) bei perkutanen Katheterisierungen mit einer 7F-Einführschleuse (2,33 mm oder kleiner) indiziert. Diese klinische Bewertung basiert auf einer umfassenden Analyse der verfügbaren klinischen Daten und Literatur vor und nach dem Inverkehrbringen, die für die vorgesehene Verwendung des FemoSeal™ VCS relevant sind.

Eine umfassende Überprüfung der veröffentlichten Literatur wurde für den Zeitraum vom 1. September 2019 bis zum 31. August 2024 durchgeführt. Die Evidenz umfasste 29 Studien für das FemoSeal™ VCS. Die in der klinischen Bewertung enthaltenen Nachweise lassen darauf schließen, dass das Prüfprodukt bei bestimmungsgemäßer Verwendung sicher und wirksam ist und dass alle Risiken oder unerwünschten Nebenwirkungen, die mit dem Produkt unter normalen Verwendungsbedingungen verbunden sein können, akzeptable Risiken darstellen, wenn die Vorteile für den Patienten abgewogen werden. Die Ergebnisse in Bezug auf die Leistung der Prüfprodukte entsprechen denen, die bei bestimmungsgemäßer Verwendung für diesen Produkttyp zu erwarten sind.

Zu den potenziellen unerwünschten Nebenwirkungen, die mit der Verwendung von FemoSeal™ VCS verbunden sind, gehören die unerwünschten Ereignisse, die häufig bei alternativen Methoden des Arterienverschlusses berichtet werden, z. B. Blutungen und Hämatome. Insgesamt ähneln die Häufigkeiten der unerwünschten Ereignisse, die bei der Verwendung von FemoSeal™ VCS gemeldet wurden, den Raten, die bei der manuellen Kompression und ähnlichen Gefäßverschlussverfahren gemeldet wurden. Insbesondere bei Blutungen und Hämatomen liegen die berichteten Raten beim FemoSeal™ VCS unter den berichteten Raten für ähnliche Gefäßverschlussverfahren. Jedes der gemeldeten unerwünschten Ereignisse, sowohl aus der veröffentlichten Literatur als auch aus der Überwachung nach dem Inverkehrbringen, war zuvor identifiziert worden (siehe **Abschnitt 1.3**).

Die vorhandenen Daten zur klinischen Sicherheit und Leistung des FemoSeal VCS deuten darauf hin, dass der Nutzen des Gefäßverschlusses für den Patienten gegenüber möglichen Risiken überwiegt, wenn es in Übereinstimmung mit der Bedienungsanleitung verwendet wird.

Wie in den vorherigen Abschnitten angegeben, zeigen die für das FemoSeal™ VCS bereitgestellten Daten die Übereinstimmung zwischen den Daten in Bezug auf das zu bewertende Produkt (z. B. Verwendung des Produkts, Ergebnisse in Bezug auf Sicherheit, klinische Leistung und klinischer Nutzen), ermittelte gleichwertige Produkte und die Daten in Bezug auf ähnliche Produkte, die im Stand der Technik aufgeführt sind.

Die Kreuzanalyse der Sicherheitsdaten ergab keine Lücken zwischen:

- im Stand der Technik erwähnten Daten,
- für das zu bewertende Produkt spezifischen Daten,

- in der/den Risikomanagementdatei(en) erwähnten Daten,
- in der Kennzeichnung und/oder Gebrauchsanweisung erwähnten Daten (d. h. man befasst sich mit den dem Benutzer zu übermittelnden Restrisiken).

Die klinische Sicherheit wurde nachgewiesen durch die niedrigen Komplikationsraten, die in der nach dem Peer-Review-Verfahren überprüften klinischen Fachliteratur, den vom Unternehmen gesponserten klinischen Studien, der Überprüfung der Daten nach dem Inverkehrbringen ermittelt wurden, sowie die Tatsache, dass es keine Marktrücknahmen gab. Es wurden keine Bedenken hinsichtlich der Leistung festgestellt. Die überprüfte Literatur enthielt eine Verwendung des FemoSeal™ VCS, die dem Verwendungszweck des Herstellers entsprach.

### **1.5 Mögliche diagnostische oder therapeutische Alternativen**

Traditionell wird die manuelle Kompression angewandt, um nach Gefäßkatheterisierungen eine Hämostase an der Arteriotomiestelle zu erreichen. Die manuelle Kompression ist mit einer langen Immobilisierung des Patienten (bis zu 8 Stunden nach einem Eingriff) sowie mit erheblichen Beschwerden und einem längeren Krankenhausaufenthalt verbunden. Eine kürzlich durchgeführte systematische Auswertung ergab, dass die mediane Zeit bis zur Hämostase bei manueller Kompression 20,8 Minuten beträgt.<sup>1</sup>

Zu den Alternativen zur manuellen Kompression gehören externe hämostatische Vorrichtungen, die eine mechanische Kompression auf die Arteriotomiestelle ausüben. Diese Vorrichtungen verkürzen nicht die Zeit bis zur Hämostase oder zur Mobilisierung, sondern reduzieren den Personalbedarf, indem sie die manuelle Kompression durch eine mechanische Kompression ersetzen. Unerwünschte Ereignisse im Zusammenhang mit einer mechanischen Kompression sind ähnlich wie bei der manuellen Kompression.

Gefäßverschlussvorrichtungen wie FemoSeal™ VCS sind für den Verschluss nach einer Arteriotomie vorgesehen. Sie zielen darauf ab, die Zeit bis zur Hämostase zu verkürzen und eine frühere Mobilisierung zu ermöglichen. Eine kürzlich durchgeführte systematische Auswertung, bei der 13 im Handel erhältliche Produkte berücksichtigt wurden, ergab, dass die mediane Zeit bis zum Erreichen der Hämostase mit einem Gefäßverschlussprodukt 5,4 Minuten beträgt. Die mediane Hämostasezeit für die einzelnen Gefäßverschlussvorrichtungen lag zwischen 1 Minute (FemoSeal™ VCS) und 14 Minuten, wobei die Mehrzahl der Produkte zwischen 4 und 10 Minuten lag.<sup>1</sup>

Häufig gemeldete unerwünschte Ereignisse im Zusammenhang mit dem Verschluss der Arteriotomiestelle – mithilfe manueller Kompression, externer hämostatischer Vorrichtungen oder Gefäßverschlussvorrichtungen – sind unter anderem: Hämatome, Blutungen an der Zugangsstelle, Pseudoaneurysmen, arteriovenöse Fisteln und Infektionen. Dieselbe systematische Auswertung (34 randomisierte kontrollierte Studien, 14.401 Patienten) ergab, dass die Rate der unerwünschten Ereignisse zwischen der manuellen Kompression und der

Verwendung von Gefäßverschlussvorrichtungen ähnlich ist, mit der Ausnahme, dass die Blutungswahrscheinlichkeit bei Gefäßverschlussvorrichtungen tendenziell etwas höher ist.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, S. 32–44.*

## 1.6 Empfohlenes Anwenderprofil und Schulung

Vorgesehene Anwender des FemoSeal™ Vascular Closure Systems sind Ärztinnen und Ärzte mit der erforderlichen Qualifizierung, um arterielle Zugänge und Verschlüsse bei endovaskulären Eingriffen über die A. femoralis communis herstellen zu dürfen, die an einem ärztlichen FemoSeal™ Schulungsprogramm der Terumo Medical Corporation teilgenommen haben.

## 1.7 Einschlägige vereinheitlichte und gemeinsame Normen

| Standardreferenz | Aktuelles Jahr der Konformität/Rev. | Beschreibung                                                                                                                             |
|------------------|-------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070        | 2014/AMD1:2018                      | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070     | 2014/A1:2018                        | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance     | 20. Mai 2021                        | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052       | 2015                                | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213       | 2017                                | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503       | 2020                                | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |

| Standardreferenz | Aktuelles Jahr der Konformität/Rev. | Beschreibung                                                                                                                                                             |
|------------------|-------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F2182       | 2019                                | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging                                    |
| EN ISO 13485     | 2016/A11:2021                       | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 13485        | 2016                                | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 14644-1      | 2015                                | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1   | 2015                                | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2      | 2015                                | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2   | 2015                                | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3      | 2019                                | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3   | 2019                                | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1      | 2003                                | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1   | 2003                                | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |

| Standardreferenz       | Aktuelles Jahr der Konformität/Rev. | Beschreibung                                                                                                                                  |
|------------------------|-------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14698-2            | 2003/TC1:2004                       | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| EN ISO 14698-2         | 2003/TC 1:2004                      | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| USP <788>              | Keine Angabe                        | PARTICULATE MATTER IN INJECTIONS                                                                                                              |
| EU Pharmacopeia 2.9.19 | Keine Angabe                        | Particulate Contamination: Sub-Visible Particles                                                                                              |
| IEC 62366-1            | 2015                                | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN 62366-1             | 2015                                | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN ISO 14971           | 2019/A11:2021                       | Medical devices — Application of risk management to Medical devices                                                                           |
| ISO 14971              | 2019                                | Medical devices — Application of risk management to Medical devices                                                                           |
| ASTM F1980             | 2016                                | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                                           |
| EN ISO 10993-1         | 2020                                | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                    |
| ISO 10993-1            | 2018                                | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                    |
| EN ISO 10993-2         | 2006                                | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                                                |
| ISO 10993-2            | 2006                                | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                                                |
| EN ISO 10993-3         | 2014                                | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity                          |

| Standardreferenz | Aktuelles Jahr der Konformität/Rev. | Beschreibung                                                                                                         |
|------------------|-------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| ISO 10993-3      | 2014                                | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4   | 2017                                | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4      | 2017                                | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| EN ISO 10993-5   | 2009                                | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| ISO 10993-5      | 2009                                | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| EN ISO 10993-6   | 2016                                | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |
| ISO 10993-6      | 2016                                | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |
| EN ISO 10993-10  | 2023                                | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                       |
| ISO 10993-10     | 2021                                | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                       |
| EN ISO 10993-11  | 2018                                | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                      |
| ISO 10993-11     | 2017                                | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                      |
| EN ISO 10993-12  | 2021                                | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                       |
| ISO 10993-12     | 2021                                | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                       |
| EN ISO 10993-17  | 2009                                | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances       |

| Standardreferenz | Aktuelles Jahr der Konformität/Rev. | Beschreibung                                                                                                                                                                 |
|------------------|-------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-17     | 2002                                | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                                                               |
| ISO 10993-18     | 2020/A1:2022                        | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-18  | 2020/A1:2022                        | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-23  | 2021                                | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23     | 2021                                | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382       | 2018                                | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756        | 2017                                | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>         | Keine Angabe                        | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>        | Keine Angabe                        | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72   | 2019                                | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135     | 2014/A1:2019                        | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135        | 2014/A1:2018                        | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development,                                                                               |

| Standardreferenz | Aktuelles Jahr der Konformität/Rev. | Beschreibung                                                                                                                                                    |
|------------------|-------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                  |                                     | Validation and Routine Control of a Sterilization Process for Medical Devices                                                                                   |
| EN ISO 10993-7   | 2008/A1:2022                        | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                       |
| ISO 10993-7      | 2008/A1:2019                        | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                               |
| EN 556-1         | 2024                                | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices |
| EN ISO 11737-1   | 2018/A1:2021                        | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11737-1      | 2018/A1:2021                        | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| EN ISO 11138-1   | 2017                                | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-1      | 2017                                | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| EN ISO 11138-2   | 2017                                | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 11138-2      | 2017                                | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| EN ISO 15223-1   | 2016                                | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| ISO 15223-1      | 2016                                | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |



| Standardreferenz  | Aktuelles Jahr der Konformität/Rev. | Beschreibung                                                                                                                                                               |
|-------------------|-------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN 1041           | 2008/A1:2013                        | Information supplied by the manufacturer of medical devices                                                                                                                |
| EN ISO 11607-1    | 2020/A1:2023                        | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| ISO 11607-1       | 2019/A1:2023                        | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| EN ISO 11607-2    | 2020/A1:2023                        | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ISO 11607-2       | 2019/A1:2023                        | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169        | 2016                                | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M | 2016                                | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825        | 2018                                | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096        | 2011 (R 2019)                       | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M     | 2015                                | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24      | 2021                                | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3       | 2020                                | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |

| Standardreferenz | Aktuelles Jahr der Konformität/Rev. | Beschreibung                                                                                                                                                                                                                                                  |
|------------------|-------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-8      | 2020                                | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                                                                                                                |
| MDCG 2020-7      | 2020                                | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                                                                                                             |
| MDCG 2020-6      | 2020                                | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                                                                                                          |
| MDCG 2019-9 v1   | 2022                                | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                                                                                      |
| MDCG 2019-8 v2   | 2020                                | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15     | 2020                                | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11     | 2021                                | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19     | 2021                                | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4   | 2021                                | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2      | 2019                                | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1      | 2019                                | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7      | 2018                                | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |

| Standardreferenz    | Aktuelles Jahr der Konformität/Rev. | Beschreibung                                                                                                                                                                                  |
|---------------------|-------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2018-6         | 2018                                | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746   |
| MDCG 2018-4         | 2018                                | MDCG 2018-4 Annex: UDI database<br>Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                               |
| MDCG 2018-3 v1      | 2020                                | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25        | 2021                                | Regulation (EU) 2017/745 - application of MDR requirements to ‘legacy devices’ and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2.12/2 rev.2 | 2012                                | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                        |

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### 3.0 ÄNDERUNGSHISTORIE

| SSCP-Revisionsnummer      | Datum der Veröffentlichung | Beschreibung der Änderung                                                    | Revision durch benannte Stelle validiert                                                                                                                                                                                                                                                                                                              |
|---------------------------|----------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022              | 20. Januar 2023            | Erstausgabe, nach CE-Zertifizierung gemäß MDR                                | <input checked="" type="checkbox"/> Ja<br>Validierungssprache: English<br><input type="checkbox"/> Nein (gilt nur für implantierbare Produkte der Klasse IIa und für einige IIb-Produkte (MDR, Artikel 52 (4) Absatz 2), für die der SSCP noch nicht von der benannten Stelle validiert wurde)<br><input type="checkbox"/> Sonstiges (bitte angeben): |
| SSCP-FS-2023 – Revision 1 | 15. März 2024              | Aktualisiert für den Zeitraum vom 1. Januar 2019 bis zum 31. Dezember 2023.  | <input checked="" type="checkbox"/> Ja<br>Validierungssprache: English<br><input type="checkbox"/> Nein (gilt nur für implantierbare Produkte der Klasse IIa und für einige IIb-Produkte (MDR, Artikel 52 (4) Absatz 2), für die der SSCP noch nicht von der benannten Stelle validiert wurde)<br><input type="checkbox"/> Sonstiges (bitte angeben): |
| SSCP-FS-2024 Revision 1   |                            | Aktualisiert für den Zeitraum vom 1. September 2019 bis zum 31. August 2024. | <input type="checkbox"/> Ja<br>Validierungssprache: English<br><input type="checkbox"/> Nein (gilt nur für implantierbare Produkte der Klasse IIa und für einige IIb-Produkte (MDR, Artikel 52 (4) Absatz 2), für die der SSCP                                                                                                                        |

|                            |               |                                                          |                                                                                                                                                                                                                                                                                                                                                                              |
|----------------------------|---------------|----------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                            |               |                                                          | <p>noch nicht von der benannten Stelle validiert wurde)</p> <p><input type="checkbox"/> Sonstiges (bitte angeben):</p>                                                                                                                                                                                                                                                       |
| SSCP-FS-2024<br>Revision 2 | June 20, 2025 | Überarbeitet auf Basis von NSAI-Anfragen zur Validierung | <p><input checked="" type="checkbox"/> Ja</p> <p>Validierungssprache:<br/>English</p> <p><input type="checkbox"/> Nein (gilt nur für implantierbare Produkte der Klasse IIa und für einige IIb-Produkte (MDR, Artikel 52 (4) Absatz 2), für die der SSCP noch nicht von der benannten Stelle validiert wurde)</p> <p><input type="checkbox"/> Sonstiges (bitte angeben):</p> |



**Resumen de seguridad y rendimiento clínico**  
**FemoSeal™ Vascular Closure System**

|                                                                |                                                                                              |
|----------------------------------------------------------------|----------------------------------------------------------------------------------------------|
| <b>Fabricante</b>                                              | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 EE. UU.      |
| <b>SRN del fabricante</b>                                      | US-MF-000019594                                                                              |
| <b>Representante de la<br/>dirección/PRRC</b>                  | Kimberly Feitl<br>Vice President, Quality                                                    |
| <b>Basic UDI-DI</b>                                            | 38970FS79                                                                                    |
| <b>Número EMDN</b>                                             | C900199 - Otros sistemas de hemostasia                                                       |
| <b>Clase de producto</b>                                       | Clase III                                                                                    |
| <b>Año de obtención del primer<br/>marcado CE del producto</b> | 2005                                                                                         |
| <b>Representante UE</b>                                        | Terumo Europe N.V.<br>Interleuvenlaan 40, 3001<br>Lovaina<br>Bélgica<br>SRN: BE-AR-000001433 |
| <b>Organismo notificado</b>                                    | NSAI<br>CE 0050                                                                              |

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La guía resumen de seguridad y rendimiento clínico (SSCP) tiene por objeto proporcionar acceso público a un resumen actualizado de los principales aspectos de seguridad y rendimiento clínico del FemoSeal™ Vascular Closure System (VCS).

A continuación, se ofrece un resumen de la seguridad y el rendimiento clínico del dispositivo, destinado a usuarios/profesionales sanitarios en la **sección 1.0**.

## **1.0 RESUMEN PARA USUARIOS/PROFESIONALES SANITARIOS**

La SSCP no pretende sustituir las instrucciones de uso, que son el documento principal para garantizar el uso seguro del producto, ni pretende proporcionar sugerencias de diagnóstico o tratamiento a los usuarios o pacientes previstos. La SSCP no pretende sustituir la información obligatoria de las tarjetas del implante ni de ningún otro documento obligatorio.

### **1.1 Uso previsto del producto**

#### **1.1.1 Uso previsto**

El FemoSeal™ Vascular Closure System es un producto sanitario indicado para cerrar una punción arterial después de un cateterismo percutáneo a través de la arteria femoral común.

#### **1.1.2 Indicaciones de uso**

El FemoSeal™ Vascular Closure System está indicado para cerrar la punción femoral habitual (arteriotomía) en pacientes que se hayan sometido a cateterismo percutáneo con una vaina quirúrgica de 2,33 mm (7F) o menor.

#### **1.1.3 Contraindicaciones y/o limitaciones**

El FemoSeal™ Vascular Closure System está contraindicado en pacientes con arteriotomías en las que se hayan utilizado vainas o dispositivos con un tamaño superior a 2,33 mm (7F).

#### **1.1.4 Poblaciones de pacientes objetivo**

La seguridad y eficacia del FemoSeal™ Vascular Closure System se ha establecido en pacientes de 18 años o más que se hayan sometido a cateterismo percutáneo con una vaina quirúrgica de 2,33 mm (7F) o menor.

#### **1.1.5 Poblaciones especiales de pacientes**

No se ha establecido la seguridad y eficacia del FemoSeal™ Vascular Closure System en las siguientes poblaciones de pacientes:

- Pacientes con enfermedad autoinmune preexistente
- Pacientes sometidos a trombolisis terapéutica
- Pacientes con enfermedad vascular periférica clínicamente significativa
- Pacientes con hipertensión no controlada ( $>220$  mmHg sistólica o  $>110$  mmHg diastólica)
- Pacientes con un trastorno hemorrágico, incluida trombocitopenia ( $<100\,000$  recuento de plaquetas) o anemia (Hgb  $<10$  mg/dl)

- Pacientes con un lumen interior de la arteria femoral común inferior a 5 mm
- Pacientes con insuficiencia renal o hepática
- Pacientes con otra comorbilidad relevante
- Población con orígenes raciales y/o étnicos específicos
- Pacientes con infarto de miocardio en las 72 horas siguientes
- Pacientes con injerto vascular o endoprótesis en el punto de punción
- Pacientes embarazadas o en periodo de lactancia
- Pacientes menores de 18 años

#### 1.1.6 Usuarios previstos

Los usuarios previstos del FemoSeal™ Vascular Closure System son médicos con formación que les permite realizar el acceso arterial y el cierre para procedimientos endovasculares a través de la arteria femoral común y han participado en un programa de formación médica FemoSeal™ de Terumo Medical Corporation.

## 1.2 Descripción del producto

### 1.2.1 Descripción del producto

El FemoSeal™ Vascular Closure System, fabricado por Terumo Medical Corporation (TMC), es un dispositivo de cierre vascular reabsorbible diseñado para lograr la hemostasia arterial femoral después de la cateterización percutánea a través de la arteria femoral común.

Los elementos de cierre FemoSeal™ constan de dos discos de polímero reabsorbible, la junta interior y el disco de bloqueo exterior, que se mantienen unidos mediante un multifilamento reabsorbible, así se sella mecánicamente la arteriotomía (consulte las **figuras 1.1 y 1.2**). Después de desplegarse a través de la vaina de la carcasa del cono, el disco de bloqueo exterior se apisona sobre el eje multifilamento, lo que resulta en el cierre mecánico del punto de punción entre el disco de bloqueo interior y exterior. La junta interior y el disco de bloqueo exterior se mantienen en su lugar mediante fricción en el eje multifilamento. La hemostasia se consigue por medios mecánicos. Los elementos de cierre se degradan por hidrólisis.

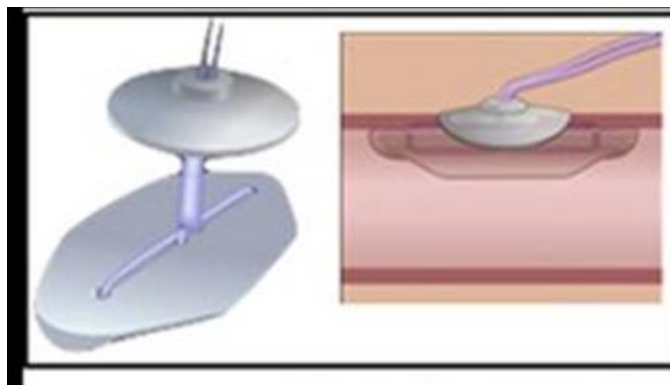
Los componentes de cierre implantables, la junta interior y el disco de bloqueo exterior se degradan en dieciocho (18) meses, mientras que se estima que el tejido circundante degrada y absorbe el multifilamento por hidrólisis después de entre dos (2) y tres (3) años. La capacidad de los componentes de cierre implantables para mantener la compresión en la arteriotomía se ha probado hasta ocho (8) horas. Los productos de degradación se metabolizan y se excretan en la orina o se

espiran como dióxido de carbono a través de los pulmones. No se han observado efectos de acumulación en estudios con animales. Los componentes adicionales de FemoSeal™ que entrarán en contacto con tejido vivo o sangre durante el procedimiento son la vaina de la carcasa del cono, el dilatador, el tubo de presión, el empujador y la guía.

**Figura 1.1 Junta interior y disco de bloqueo exterior, respectivamente**

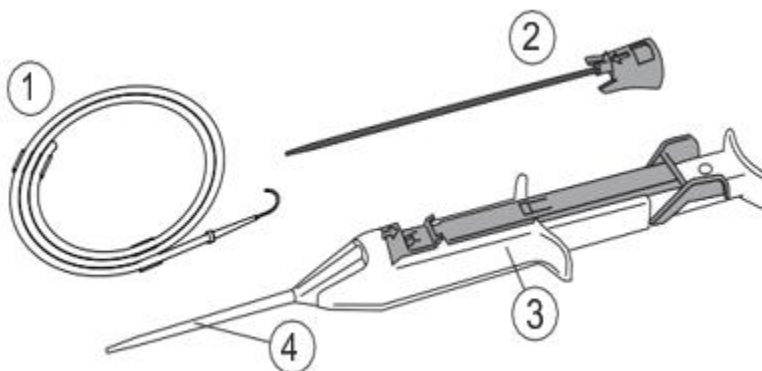


**Figura 1.2 Junta interior y disco de bloqueo exterior desplegados**



La unidad FemoSeal™ se suministra junto con un dilatador y una guía de 0,97 mm (0,038 in) de diámetro externo, 70 cm (27,5 in) de longitud y un enderezador en J. Consulte la **figura 1.3**. La guía está contenida dentro de un tubo de polietileno. Todas las piezas se embalan en una bandeja de papel fija. El envase también incluye la tarjeta del implante del paciente. El FemoSeal™ Vascular Closure System no requiere accesorios adicionales para que el producto funcione según lo previsto y solo está diseñado para su uso con el dilatador y la guía incluidos en el envase del producto.

**Figura 1.3 Unidad FemoSeal™ VCS con guía y dilatador**



### 1.2.2 Materias primas y componentes

En la **tabla 1.1** se enumeran los componentes del FemoSeal™ VCS.

**Tabla 1.1 Materias primas y componentes de FemoSeal™ VCS**

| Número de referencia | Descripción                                                  |                                                           | Materiales                                                                                                                                                                                                              |
|----------------------|--------------------------------------------------------------|-----------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1                    | Guía de 0,97 mm (0,038 in) con un enderezador en J para guía |                                                           | Guía: Acero inoxidable 304<br>Enderezador en J: polipropileno, pigmento violeta<br>Pinza: polietileno<br>Líneas: polietileno                                                                                            |
| 2                    | Dilatador FemoSeal                                           |                                                           | Conector: tetrahidrofurano, pigmento azul, tereftalato de polibutileno (PBT)<br><br>Tubo: polietileno de alta densidad (HDPE), pigmento negro<br><br>Lubricante: silicona Dow Corning 360                               |
| 3/4                  | Unidad FemoSeal                                              | RD7 moldeado: junta interior y disco de bloqueo exterior* | Copolímero entre glicólico, carbonato de trimetileno, $\epsilon$ -caprolactona y TMP: trimetilolpropano (iniciador)                                                                                                     |
|                      |                                                              | Multifilamento*                                           | Copolímero segmentado entre L,L-lactida, carbonato de trimetileno, $\epsilon$ -caprolactona y 1,3 propanodiol (iniciador)<br><br>El recubrimiento es un copolímero entre glicólico, $\epsilon$ -caprolactona y L-lisina |



|  |  |                              |                                                   |
|--|--|------------------------------|---------------------------------------------------|
|  |  | Tubo de compactación         | Polipropileno                                     |
|  |  | Empujador                    | Acero inoxidable 304V                             |
|  |  | Corredera                    | Tereftalato de polibutileno (PBT)                 |
|  |  | Carcasa                      | Tereftalato de polibutileno (PBT)                 |
|  |  | Botón                        | Tereftalato de polibutileno (PBT)                 |
|  |  | Tapa de botón                | Copolímero de polioximetileno (POM)/poliacetal    |
|  |  | Funda                        | Tereftalato de polibutileno (PBT)                 |
|  |  | Espaciador                   | Tereftalato de polibutileno (PBT)                 |
|  |  | Cono                         | Polipropileno                                     |
|  |  | Tapa de la carcasa           | Tereftalato de polibutileno (PBT)                 |
|  |  | Bloqueo de seguridad         | Tereftalato de polibutileno (PBT), pigmento azul  |
|  |  | Tapa de la funda             | Tereftalato de polibutileno (PBT)                 |
|  |  | Junta del tubo               | Silicona shore A 70                               |
|  |  | Junta de la carcasa          | Silicona shore A 50                               |
|  |  | Resorte                      | Acero inoxidable 302                              |
|  |  | Vaina de la carcasa del cono | Polipropileno<br>Silicona Dow Corning 360, hexano |

\*Parte implantable del producto; los componentes implantables son seguros para RM

El FemoSeal™ VCS se esteriliza mediante óxido de etileno (OE) y es un producto sanitario de un solo uso. El dispositivo FemoSeal™ VCS está diseñado de tal manera que no se puede reutilizar.

### **Modo de funcionamiento**

El FemoSeal™ VCS promueve la hemostasia mecánica mediante el despliegue de elementos de cierre implantables dentro y fuera de la arteria femoral común. El mecanismo que evita la hemorragia lo proporciona la junta interior, que sella el punto de punción, y el disco de bloqueo exterior, que mantiene la junta interior en su posición.

#### **1.2.3 Beneficio clínico**

El FemoSeal™ VCS proporciona los siguientes beneficios clínicos en relación con el cierre vascular después de insertar una punción femoral común:

- Reducción del tiempo de hemostasia<sup>1</sup>
- Reducción del tiempo de deambulación<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R. y Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32-44.

#### 1.2.4 Generaciones o variantes anteriores

- La primera versión de FemoSeal™ VCS (n.º 11200) se vendió en el mercado europeo durante el año 2005 y parte de 2006.
- El actual FemoSeal™ VCS (n.º 11202), con un sistema de distribución mejorado, lleva en el mercado desde el 28 de marzo de 2006.

#### 1.2.5 Accesorios diseñados para su uso en combinación con el producto

La unidad FemoSeal™ se suministra con un dilatador, una guía de 0,97 mm (0,038 in) de diámetro externo y 70 cm (27,5 in) de longitud y un enderezador en J. La guía es un accesorio de la unidad FemoSeal™. El enderezador en J es un componente de la guía, mientras que el dilatador es un componente de la unidad FemoSeal™. La guía es el único accesorio considerado. La guía está contenida dentro de un tubo de polietileno. Todas las piezas se embalan en una bandeja de papel fija. El envase también incluye la tarjeta del implante del paciente. El FemoSeal™ Vascular Closure System no requiere accesorios adicionales para que el producto funcione según lo previsto y solo está diseñado para su uso con el dilatador y la guía incluidos en el envase del producto.

#### 1.2.6 Otros dispositivos y productos previstos para su uso en combinación con el dispositivo

El FemoSeal™ VCS no requiere dispositivos adicionales para funcionar según lo previsto.

### 1.3 Riesgos y advertencias

#### 1.3.1 Riesgos residuales y efectos no deseados

Los acontecimientos adversos, daños y complicaciones conocidos o previsibles asociados con el uso del FemoSeal™ VCS como resultado del riesgo residual se enumeran en la **tabla 1.2**. La tasa de incidencia se basa en un análisis de la documentación de riesgos y se calcula en función de los datos de vigilancia posteriores a la comercialización desde el 1 de septiembre de 2019 hasta el 31 de agosto de 2024. No se conocen riesgos residuales para el FemoSeal™ VCS y todos los riesgos aplicables se han abordado mediante el suministro de las instrucciones de uso y el proceso de gestión de riesgos.

**Tabla 1.2. Acontecimientos adversos/complicaciones del FemoSeal**

| <b>Daño</b>                                           | <b>Tasa de incidencia (%)</b> | <b>Factores de mitigación</b>                                                                                                                                                                               |
|-------------------------------------------------------|-------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Reacción alérgica                                     | 0,0000                        | Las acciones y los planes para reducir el riesgo al mínimo posible se han abordado mediante características de diseño del producto, directrices de fabricación, etiquetado del producto y formación médica. |
| Aneurisma                                             | 0,0000                        |                                                                                                                                                                                                             |
| Fístula AV                                            | 0,0001                        |                                                                                                                                                                                                             |
| Pérdida de sangre, hemorragia                         | 0,0280                        |                                                                                                                                                                                                             |
| Muerte                                                | 0,0002                        |                                                                                                                                                                                                             |
| Equimosis                                             | 0,0000                        |                                                                                                                                                                                                             |
| Embolia                                               | 0,0000                        |                                                                                                                                                                                                             |
| Reacción a cuerpos extraños                           | 0,0000                        |                                                                                                                                                                                                             |
| Hematomas                                             | 0,0027                        |                                                                                                                                                                                                             |
| Hemorragias                                           | 0,0001                        |                                                                                                                                                                                                             |
| Infección                                             | 0,0002                        |                                                                                                                                                                                                             |
| Reacción inflamatoria                                 | 0,0000                        |                                                                                                                                                                                                             |
| Entumecimiento                                        | 0,0000                        |                                                                                                                                                                                                             |
| Dolor                                                 | 0,0000                        |                                                                                                                                                                                                             |
| Malestar del paciente                                 | 0,0004                        |                                                                                                                                                                                                             |
| Retraso del procedimiento                             | 0,0065                        |                                                                                                                                                                                                             |
| Pseudoaneurisma                                       | 0,0004                        |                                                                                                                                                                                                             |
| Hemorragia retroperitoneal                            | 0,0002                        |                                                                                                                                                                                                             |
| Sepsis                                                | 0,0000                        |                                                                                                                                                                                                             |
| Tromboembolia                                         | 0,0000                        |                                                                                                                                                                                                             |
| Trombosis                                             | 0,0001                        |                                                                                                                                                                                                             |
| Oclusión de vasos/isquemia de extremidades inferiores | 0,0002                        |                                                                                                                                                                                                             |
| Perforación de vasos                                  | 0,0000                        |                                                                                                                                                                                                             |
| Disección/laceración del tejido vascular              | 0,0003                        |                                                                                                                                                                                                             |

### 1.3.2 Advertencias y precauciones

#### Advertencias

1. No lo utilice si el envase está dañado o si alguna barrera estéril no está intacta.
2. No lo utilice después de la fecha de caducidad, ya que es posible que los componentes biodegradables no funcionen correctamente.
3. No lo utilice si alguno de los elementos parece dañado o defectuoso.
4. El uso del FemoSeal™ Vascular Closure System en los casos en los que se haya producido contaminación bacteriana de la vaina quirúrgica o del tejido circundante puede provocar una infección.
5. Si se sospecha que se ha insertado la pared posterior de la arteria o que se ha realizado más de una punción arterial, no confíe únicamente en el FemoSeal™ Vascular Closure System para conseguir la hemostasia arterial. Utilice compresión manual o mecánica adicional.
6. Si el punto de punción se encuentra en la bifurcación de la arteria femoral o distal a ella, el FemoSeal™ Vascular Closure System no debe utilizarse debido al riesgo de que la junta interior se coloque de forma incorrecta. Este acontecimiento puede provocar hemorragias y/o interrumpir el flujo sanguíneo normal.
7. Si hay una hemorragia arterial persistente en el lugar de la incisión, no corte el multifilamento hasta lograr la hemostasia. Si no se logra la hemostasia, fije el multifilamento con un apósito estéril y aplique compresión suplementaria hasta lograr la hemostasia. En caso de hemorragia arterial persistente, pueden producirse complicaciones significativas del sangrado que podrían provocar lesiones en el paciente o su muerte.
8. No utilice el FemoSeal™ Vascular Closure System si el punto de punción está próximo al ligamento inguinal, ya que esto podría provocar un hematoma retroperitoneal.
9. Los pacientes con un mayor riesgo de hemorragia pueden sufrir una mayor pérdida de sangre y requerir una transfusión.
10. Si el disco interior se desprende, puede causar un evento trombótico y/o embólico.

#### Precauciones

1. El procedimiento de despliegue del FemoSeal™ Vascular Closure System debe ser realizado por médicos con la formación adecuada en el uso del producto.
2. Realice un angiograma femoral limitado o una punción femoral guiada por ecografía antes de desplegar el FemoSeal™ Vascular Closure System.
3. Interrumpa el procedimiento en los siguientes casos:

- Diámetro del lumen de la arteria femoral común <5 mm
  - Estenosis y/o placa significativa presente en las proximidades del punto de punción femoral común
  - Punción arterial insertada en la bifurcación de la arteria femoral o distal a ella
  - Ramas o vasos anómalos presentes cerca del punto de punción femoral común
4. Si existe un hematoma, se debe tener especial cuidado para la correcta inserción de la vaina del cono en la arteria.
  5. Utilice una técnica de punción de pared única. No perfora la pared posterior de la arteria.
  6. Observe la técnica estéril en todo momento cuando utilice el FemoSeal™ Vascular Closure System.
  7. El FemoSeal™ Vascular Closure System es de un solo uso y no se debe volver a esterilizar ni a utilizar de ninguna manera. La unidad FemoSeal™ está diseñada de tal manera que no se puede reutilizar.
  8. Si el despliegue de la junta interior encuentra una resistencia inesperada, interrumpa el procedimiento.
  9. Para desplegar correctamente la junta interior, vuelva a colocar el pulgar de modo que el botón pueda retroceder libremente.
  10. Asegúrese de que la punta de la vaina de la carcasa del cono de la unidad FemoSeal™ esté debajo de la superficie de la piel antes de desplegar el disco de bloqueo exterior. El disco de bloqueo exterior puede desplegarse involuntariamente por encima del nivel de la piel en pacientes con una distancia corta entre la arteria femoral y el nivel de la piel.
  11. Para un despliegue correcto, puede ser necesaria una incisión cutánea antes del despliegue.
  12. Si la junta interior está dentro de la arteria, pero no es posible presionar completamente el botón y desplegar el disco de bloqueo exterior, puede ser necesaria una cirugía para retirar los elementos de cierre FemoSeal™.
  13. Si fuera necesario volver a perforar la misma arteria femoral en un plazo de 18 meses, debe volver a practicarse la punción al menos un centímetro proximal al punto de acceso anterior del FemoSeal™ Vascular Closure System.
  14. Indique al paciente que siga las indicaciones del médico con respecto a la inspección del lugar de cierre.
  15. Indique al paciente que lleve consigo la tarjeta de información para el paciente durante los próximos 18 meses.

**Precauciones en el momento del alta**

Antes de considerar el alta, evalúe al paciente para detectar las siguientes condiciones clínicas:

- 1. Hemorragia y/o hematoma en el lugar de cierre
- 2. Dolor al caminar
- 3. Signos de infección en el lugar de cierre

**1.3.3 Acciones correctivas de seguridad**

Hubo una acción correctiva de seguridad relacionada con el FemoSeal™ VCS durante el periodo comprendido entre el 1 de septiembre de 2019 y el 31 de agosto de 2024.

En 2022, Terumo retiró voluntariamente el FemoSeal™ VCS debido a la existencia de quejas que alegaban fallos en las pruebas de proceso y liberación de lotes del producto FemoSeal fabricado por Elkton para la medición de la fuerza de compactación y la fuerza de retracción. Se retiraron un total de 950 unidades en Corea del Sur.

**1.4 Evaluación clínica y del seguimiento clínico posterior al lanzamiento**

La **tabla 1.3** incluye una lista de estudios fundamentales incluidos para introducir el FemoSeal™ VCS en el mercado, así como estudios posteriores a la comercialización y actividades de seguimiento clínico posteriores a la comercialización. La versión del dispositivo utilizada en el estudio se incluye en la siguiente tabla. La primera versión del FemoSeal™ VCS (n.º 11200) estuvo en el mercado hasta 2006, mientras que la siguiente versión (n.º C11202) se lanzó al mercado en 2006 y es la que está actualmente en el mercado.

**Tabla 1.3 Resumen de estudios fundamentales**

| Pruebas funcionales con animales previas a la comercialización                                                                                                                                                                                                          | Versión del dispositivo |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                   |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                   |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                   |
| Primer estudio clínico en seres humanos                                                                                                                                                                                                                                 |                         |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                   |

| Estudios clínicos posteriores a la comercialización finalizados                                                                 |                                |
|---------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                      | C11202<br>(dispositivo actual) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                               | C11202<br>(dispositivo actual) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | C11202<br>(dispositivo actual) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)          | C11202<br>(dispositivo actual) |
| Estudios clínicos posteriores a la comercialización planificados/en curso                                                       |                                |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                      | C11202<br>(dispositivo actual) |
| Actividades de seguimiento clínico posterior a la comercialización                                                              |                                |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(dispositivo actual) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(dispositivo actual) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(dispositivo actual) |

#### 1.4.1 Resumen de los datos (de investigaciones clínicas y pruebas en animales) previas a la comercialización

En la **tabla 1.4** se describen todos los estudios previos a la comercialización, tanto pruebas en animales como investigaciones clínicas.

**Tabla 1.4 Resúmenes de estudios previos a la comercialización**

| Pruebas funcionales con animales previas a la comercialización                                                    |                                |                                                 |                                                                                                                                  |                                                                                                                         |                                                                                                                                                                                                                               |
|-------------------------------------------------------------------------------------------------------------------|--------------------------------|-------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Nombre del estudio                                                                                                | Año/IC                         | Tipo de estudio                                 | Objetivos                                                                                                                        | Hitos                                                                                                                   | Criterios de aceptación potencial                                                                                                                                                                                             |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculture System. | 2000<br>Radi Medical System AB | Estudio en animales; investigación exploratoria | El objetivo del estudio era evaluar la biocompatibilidad y biofuncionalidad de un implante biodegradable diseñado para lograr la | N = 3 ovejas adultas, 1 animal por punto de evaluación<br><br>Seguimiento del análisis histopatológico, la calificación | Permeabilidad arterial <ul style="list-style-type: none"> <li>Evaluación del flujo sanguíneo posterior a la implantación: 2/3 de reducción del flujo sanguíneo relacionada con el vasoespasma arterial provisional</li> </ul> |

|                                                                                                                                                      |                                  |  |                                                                                                                            |                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|--|----------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | Realizado por Biomatech, Francia |  | hemostasia en el sistema vascular. El informe aborda animales de reserva del estudio número 862 (n.º de documento 1051-01) | <p>macroscópica y el análisis ultraestructural</p> <ul style="list-style-type: none"> <li>12 meses</li> <li>15 meses</li> <li>18 meses</li> </ul> <p>Seguimiento por ecografía Doppler en color: 30 días en los puntos de acceso arterial femoral y carotídeo</p> | <p>atribuido al procedimiento, ambos se produjeron en la arteria carótida común izquierda</p> <ul style="list-style-type: none"> <li>Evaluación ecográfica Doppler en color (4 semanas): 3/3 (100 %) sin reducción importante del flujo sanguíneo 30 días después de la implantación</li> </ul> <p>Observaciones macroscópicas</p> <ul style="list-style-type: none"> <li>12 meses: permeabilidad macroscópica confirmada por ausencia de oclusión anatómicamente visible; no se observaron lesiones macroscópicas de intolerancia local (hemorragia, necrosis o neovascularización); se observó marcado el encapsulamiento del disco interno</li> <li>15 meses: la observación macroscópica no mostró signos de inflamación; no se identificaron residuos de discos internos o externos; el tejido de encapsulación ubicado en el área del disco externo parecía el mismo que en la observación de los 12 meses</li> <li>18 meses: la observación macroscópica no mostró signos de intolerancia local, disco exterior visible (3/3 casos), degradación del disco interior completa; 1/3 (arteria carótida común izquierda): depresión de la pared arterial observada en el lugar del implante (podría estar relacionada con el despliegue del dispositivo)</li> </ul> <p>Conclusiones</p> <ul style="list-style-type: none"> <li>Macroscópicamente, 12, 15 y 18 meses después de la implantación no se detectaron signos necróticos, degenerativos ni trombóticos.</li> </ul> |
|------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|--|----------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|



|                                                                                                                                                                                                                                                                         |                                                                      |                                                 |                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------|-------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                                                                                         |                                                                      |                                                 |                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                       | <ul style="list-style-type: none"> <li>El proceso de degradación de los discos interiores y exteriores pareció progresar entre los 12 y los 18 meses y parecía completo a los 18 meses, con un tejido blanquecino que cubría el área implantada.</li> <li>Histológicamente, después de 18 meses, el material polimérico ya no era visible, pero había un tejido fibroso endoluminal presente. No se observaron lesiones necróticas, degenerativas ni trombóticas.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 2002 Radi Medical System AB.<br><br>Realizado por Biomatech, Francia | Estudio en animales; investigación exploratoria | El objetivo del estudio era evaluar la biocompatibilidad de un implante biodegradable diseñado para lograr la hemostasia en el sistema vascular. | Seguimiento (después de la implantación) <ul style="list-style-type: none"> <li>12 semanas</li> <li>24 semanas</li> <li>36 semanas</li> </ul> <p>N = 12 ovejas, 3 animales por punto de evaluación, 3 animales de reserva sacrificados a los 12, 15 y 18 meses</p> <p>Lugares de implantación: arterias femorales derecha e izquierda, arterias carótidas comunes derecha e izquierda</p> <p>Análisis ecográfico doppler en color</p> | <u>Permeabilidad de las arterias carótida y femoral después de 4 semanas</u> <ul style="list-style-type: none"> <li>Reducción importante del flujo sanguíneo 0/12 (0 %)</li> </ul> <p><u>Sin reducción importante del flujo sanguíneo</u></p> <ul style="list-style-type: none"> <li>Insuficiencia grave del flujo sanguíneo relacionada con la introducción del dispositivo 0/12 (0 %)</li> <li>Reducción del flujo sanguíneo en la carótida común izquierda 2/12 (16,6 %) debido a un vasoespasmio arterial provisional (atribuido a la cirugía, no al dispositivo)</li> </ul> <p><u>Deterioro del flujo sanguíneo por seguimiento</u></p> <p>12 semanas – 0/12 (0 %)<br/> 24 semanas – 0/12 (0 %)<br/> 36 semanas – 0/12 (0 %)</p> <p>Medición de la presión arterial (3 ovejas - 36 semanas)</p> <ul style="list-style-type: none"> <li>No se ha detectado una reducción importante del flujo sanguíneo</li> </ul> |

|  |  |  |  |  | <p>Datos macroscópicos para la integración y degradación (grado 0-4)</p> <p><u>Sitios carotídeos</u></p> <p><i>Cara interior</i></p> <p>-encapsulado</p> <p>12 semanas 1,3</p> <p>24 semanas 0,8</p> <p>36 semanas 0,7</p> <p>-degradación del material</p> <p>12 semanas 2,2</p> <p>24 semanas 2,3</p> <p>36 semanas 0,7</p> <p><i>Cara exterior</i></p> <p>-encapsulado</p> <p>12 semanas 2,0</p> <p>24 semanas 1,0</p> <p>36 semanas 0,8</p> <p>-degradación del material</p> <p>12 semanas 2,0</p> <p>24 semanas 2,7</p> <p>36 semana 3,2</p> <p><u>Sitios femorales</u></p> <p><i>Cara exterior</i></p> <p>-encapsulado</p> <p>12 semanas 1,0</p> <p>24 semanas 2,7</p> <p>36 semanas 1,0</p> <p>-degradación del material</p> <p>12 semanas 2,0</p> <p>24 semanas 2,4</p> <p>36 semanas 3,0</p> <p><i>Cara interior</i></p> <p>-encapsulado</p> <p>12 semanas 2,0</p> <p>24 semanas 1,2</p> <p>36 semanas 1,0</p> <p>-degradación del material</p> <p>12 semanas 1,0</p> <p>24 semanas 2,2</p> <p>36 semanas 3,0</p> <p><u>Datos histológicos para la integración, degradación y parámetros inflamatorios (media de valores relevantes, índice 0-4) n=6</u></p> |
|--|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | <u>Sitios carotídeos</u><br>Fibrosis externa<br>12 semanas – 2,3<br>24 semanas – 2,3<br>36 semanas – 1,8<br>Neoíntima interna<br>12 semanas – 3,0<br>24 semanas – 2,7<br>36 semanas – 3,3<br>Degradación del material<br>12 semanas – 1,7<br>24 semanas – 3,0<br>36 semanas – 3 +<br>Parámetros inflamatorios (macrófagos)<br>12 semanas – 3,0<br>24 semanas – 1,7<br>36 semanas –1,7<br><u>Sitios femorales</u><br>Fibrosis externa<br>12 semanas – 1,3<br>24 semanas – 1,5<br>36 semanas –1,7<br>Neoíntima interna<br>12 semanas – 3,7<br>24 semanas – 3,3<br>36 semanas – 3,8<br>Degradación del material<br>12 semanas – 2,0<br>24 semanas – 3,0<br>36 semanas – 3+<br>Parámetros inflamatorios (macrófagos)<br>12 semanas – 3,5<br>24 semanas – 1,8<br>36 semanas – 1,8<br><br><u>Valores de permeabilidad histomorfológica</u><br>Sitios carotídeos<br>12 semanas 74,0 %<br>24 semanas 81,9 %<br>36 semanas -89,43 %<br>Sitios femorales<br>12 semanas - 42,2 %<br>24 semanas - 73,21 %<br>36 semanas - 78,71 %<br><br><u>Permeabilidad de los vasos en EE. UU. (% medio)</u><br>Sitios carotídeos |
|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                                                                                                                                                                                                                                                                 |                                                                            |                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
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|                                                                                                                                                                                                                                                                 |                                                                            |                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                        | 12 semanas 94,6 %<br>24 semanas - 96,7 %<br>36 semanas - 94,7 %<br>Sitios femorales<br>12 semanas - 66,9 %<br>24 semanas - 63,6 %<br>36 semanas - 75,1 %<br><br>Conclusiones <ul style="list-style-type: none"> <li>No se detectó ningún signo de intolerancia local significativo (ausencia de lesiones inflamatorias, necróticas o degenerativas visibles) a las 12, 24 o 36 semanas</li> <li>No se registró ninguna reacción tisular adversa significativa con respecto al huésped y al dispositivo</li> <li>La degradación del implante casi se completó a las 36 semanas</li> </ul>                        |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France). | 2002<br><br>Radi Medical System AB<br><br>Realizado por Biomatech, Francia | Estudio en animales | El propósito del estudio consistía en evaluar la biocompatibilidad y biofuncionalidad de un implante biodegradable diseñado para lograr la hemostasia en el sistema vascular. El dispositivo sometido a prueba estaba destinado a insertarse en el orificio perforado en las arterias para lograr la hemostasia. Un disco entró en el orificio insertado en la arteria y el otro apretó el disco interno desde el exterior de la arteria. Ambos discos se insertaron a través de una vaina introductora. Los discos se diseñaron para prevenir hemorragias, para curarse en la pared del vaso y finalmente degradarse y absorberse. El estudio se diseñó para recopilar y analizar datos | El periodo de implantación/seguimiento es de 5 semanas para todos los animales<br><br>4 ovejas, 1 cerdo<br><br>14 elementos de cierre<br><br>8 elementos de cierre implantados en 2 ovejas<br><br>2 elementos de cierre implantados en 1 cerdo<br><br>Cuando se implantaron dos elementos de cierre en la misma arteria femoral, se implantaron a una distancia >30 mm | Se registró todo criterio de signos adversos (inflamación, necrosis, hemorragia o cualquier otra lesión) y toda formación de capa pseudointimal delgada. Se prestó especial atención a la integración tisular inicial del dispositivo, con especial atención a la encapsulación interna del disco.<br><br>Macroscópicamente, no se observaron signos significativos de intolerancia local ni formación de trombos. La observación macroscópica no reveló ninguna diferencia entre la oveja o el cerdo después de la implantación de los elementos de cierre en las arterias femorales. Macroscópicamente, no se |

|  |  |  | después de la implantación funcional en ovejas y cerdos con el fin de evaluar la capacidad del implante para mantener la función fisiológica cuando se utiliza en el sistema circulatorio, determinar la respuesta del huésped y la respuesta del dispositivo (integridad física, encapsulación tisular en el sacrificio) y evaluar la degradación del implante. |  | <p>observaron signos significativos de intolerancia local ni formación de trombos. La observación macroscópica no reveló ninguna diferencia entre la oveja o el cerdo después de la implantación de los elementos de cierre en las arterias femorales.</p> <p>El análisis histopatológico del lugar de implantación en ovejas no mostró reacciones adversas locales. Los discos interior y exterior mostraron signos de degradación y, en algunos casos, se rompieron en partes más pequeñas. Los discos internos se integraron completamente en el tejido neointimal. En el cerdo, el análisis histopatológico mostró ligeramente más signos inflamatorios alrededor de los discos interiores y exteriores. En ambos animales, el multifilamento exhibió ligeramente más signos inflamatorios que en el material de disco, lo cual es normal para las suturas trenzadas debido a la mayor dimensión de la zona superficial.</p> <p>La permeabilidad del vaso se midió después de cinco semanas por medio del uso de tres métodos diferentes, histomorfométrico, histomorfométrico en combinación con la medición del diámetro del vaso por medio del uso del calibre y por medio del uso</p> |
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|                                                                                                                                                                                                              |                              |                                               |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                            | de la ultrasonografía doppler en color. La permeabilidad media de los vasos en ovejas fue de entre el 60 y el 80 %, según el método (12 observaciones). En el cerdo, la permeabilidad media del vaso fue de entre el 40 y el 80 % (2 observaciones).                                                                                                                                                                                                                                                                                                                                                                                                      |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-----------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Primer estudio clínico en seres humanos</b>                                                                                                                                                               |                              |                                               |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Nombre del estudio                                                                                                                                                                                           | Año/IC                       | Tipo de estudio                               | Objetivos                                                                                                                                                                                                                                                                                                                                       | Hitos                                                                                                                                                                                                                                                                                                                                                                                                      | Criterios de aceptación potencial                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Ensayo multicéntrico abierto de un solo grupo | El estudio tenía como objetivo determinar la seguridad, el rendimiento y la eficacia del FemoSeal Vascular Closure System (sistema FemoSeal) en general y, específicamente, de los elementos de cierre, en pacientes sometidos a procedimientos cardiológicos de diagnóstico cardíaco o intervencionistas mediante acceso a la arteria femoral. | <p>Estudio en dos partes</p> <p>Total n = 80</p> <p>Parte 1 n = 20</p> <p>Parte 2 n = 60</p> <p>Indicaciones:</p> <p>Parte 1: cateterización cardíaca diagnóstica utilizando la arteria femoral como lugar de acceso</p> <p>Parte 2: pacientes sometidos a procedimientos cardíacos de diagnóstico e intervención que utilizan la arteria femoral como lugar de acceso</p> <p>Seguimiento tras 30 días</p> | <p>Resultados</p> <p><u>-hemostasia lograda con FS sin compresión</u></p> <p>- Parte 1 20/20 (100 %)</p> <p>- Parte 2 58/60 (97 %)</p> <p>Tiempo medio hasta la hemostasia en el momento del procedimiento (parte 2): 1,0 minutos (intervalo inmediato: 8 minutos)</p> <p><u>Tiempo hasta la deambulacion (minutos)</u></p> <p>Parte 1</p> <p>Medio: 33,0</p> <p>media: 67,8</p> <p>Parte 2</p> <p>medio: 45</p> <p>media: 87,5</p> <p><u>Incidencia de complicaciones vasculares importantes: seguimiento a los 30 días</u></p> <p>Parte 1</p> <p>-Sin complicaciones vasculares 20/20 (100 %)</p> <p>Parte 2</p> <p>Pseudoaneurisma - 1/59 (1,69 %)</p> |

|  |  |  |  |  | <u>Fracaso del tratamiento</u><br>Parte 1 - 0/20 (0 %)<br>Parte 2 - 3/60 (5 %) <ul style="list-style-type: none"> <li>2 por no lograr la hemostasia sin el uso de compresión</li> <li>1 por complicación vascular importante, pseudoaneurisma</li> </ul><br><u>Exudado persistente</u><br>Parte 1 - 0/20 (0 %)<br>Parte 2 - 8/60 (13 %)<br><u>Hematoma</u><br>Parte 1 - 0/20 (0 %)<br>Parte 2 - 6/60 (10 %) |
|--|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Como parte del plan de desarrollo previo a la comercialización del FemoSeal™ VCS, se realizaron tres pruebas funcionales en animales. En el 2000, antes de iniciar los estudios clínicos, se realizó un estudio en animales para evaluar la biofuncionalidad del FemoSeal™ VCS. Este estudio evaluó la capacidad de los elementos de cierre para mantener la función fisiológica y evaluar su degradación. A los 18 meses, el material del disco interior y exterior ya no era visible, después de haber sido reemplazado con un tejido fibroso endoluminal. En conclusión, se confirmó la capacidad del elemento de cierre FemoSeal™ VCS para mantener la función fisiológica cuando se utiliza en el sistema circulatorio.

En 2002 se realizó un estudio en animales para evaluar la biocompatibilidad y biofuncionalidad de un implante biodegradable, FemoSeal™ VCS, diseñado para lograr la hemostasia en el sistema vascular. En resumen, la degradación del implante casi se completó a las 36 semanas y no hubo una reacción tisular adversa significativa.

Otro estudio en animales en 2002 evaluó la biocompatibilidad y biofuncionalidad de un implante biodegradable, FemoSeal™ VCS, diseñado para lograr la hemostasia en el sistema vascular. Después de 5 semanas, la encapsulación del disco se completó, y se observaron signos de degradación para los discos internos y externos. En conclusión, se confirmó la capacidad del implante para mantener la función fisiológica cuando se utilizó en el sistema circulatorio.

Como parte del plan de desarrollo clínico para el FemoSeal™ VCS, Radi Medical System AB llevó a cabo una investigación clínica previa a la comercialización. Esta investigación clínica no está publicada ni disponible en línea. El estudio con el dispositivo modelo n.º 11200 se llevó a

cabo en 2002-2004 según la norma europea EN 540 (Clinical Investigation of Medical Devices for Human Subjects) y de acuerdo con «ICH General Considerations for Clinical Trials and Guideline for Good Clinical Practice». Los detalles de este estudio se documentan en el informe EU-SE-001. El estudio clínico se documentó en el informe final de Radi Medical Systems AB, «Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures». El estudio clínico se realizó con el primer modelo n.º 11200 de FemoSeal™ y se centró en la seguridad y efectividad de los componentes de cierre implantables. La única diferencia entre el primer modelo n.º 11200 y el modelo actual (C11202) es el tamaño francés, 6F y 7F respectivamente, y el sistema de distribución mejorado. Los beneficios clínicos, el uso previsto, los fundamentos de la operación y las materias primas de los elementos de cierre implantables, el sellado interior y el disco de bloqueo exterior permanecen sin cambios.

El uso previsto del dispositivo fue para pacientes que se sometieron a procedimientos cardíacos de diagnóstico o intervencionistas en los que se utilizó la arteria femoral como punto de acceso. El objetivo de este estudio era determinar la seguridad, el rendimiento y la eficacia del FemoSeal™ VCS. Se trataba de un estudio prospectivo, multicéntrico, de un solo grupo, abierto y con seguimiento a los 30 días.

El criterio de valoración principal del rendimiento fue el tiempo hasta la hemostasia definido como la ausencia de hemorragia rápida. El criterio de valoración principal de la seguridad fue la incidencia de complicaciones vasculares importantes durante 30 días. Los criterios secundarios de valoración incluyeron el tiempo hasta la deambulación, la proporción de fracasos del tratamiento, la incidencia de eventos adversos y las características de rendimiento del dispositivo durante la dispensación y el despliegue.

Los pacientes incluidos en este estudio fueron adultos capaces de dar su consentimiento informado y con al menos un pulso pedio intacto. Los pacientes fueron excluidos del estudio si presentaban alguna de las siguientes afecciones:

- Antecedentes de enfermedad vascular periférica
- Enfermedad autoinmune
- Trastorno hemorrágico conocido de anemia grave
- INR >1,5
- Infarto de miocardio a las 72 horas
- Hipertensión no controlada a pesar del tratamiento
- Obesidad que impide el acceso con la técnica de Seldinger
- Presencia de injerto vascular o stent en el lugar de la arteriotomía



- Punción ipsilateral previa insertada en un plazo de 3 meses
- Esperanza de vida prevista <6 meses

Además, se examinó a los pacientes de forma intraoperatoria y se excluyeron del estudio si se observaba alguna de los siguientes síntomas:

- Diámetro del lumen de la arteria femoral común <5 mm
- Ramas arteriales a menos de 2 cm del punto de punción
- Estenosis significativa a menos de 3 cm del punto de punción
- Uso de la vaina introductora principal >6 F
- Punción en o distal a la bifurcación femoral
- Múltiples punciones femorales
- Punción conocida o sospechada de la pared femoral posterior
- Hematoma grande (2:6 cm) al finalizar el procedimiento
- Dificil inserción de la vaina primaria para el procedimiento debido a tejido tortuoso o vaso

Este estudio de protocolo único se llevó a cabo en dos partes: en la primera parte participaron 20 pacientes; a continuación, se completó un análisis de seguridad y luego participaron 60 pacientes adicionales durante la segunda parte.

En la primera parte, la edad media de los pacientes participantes era de 65,9 años, el 70,0 % de los pacientes eran varones y el 95 % de los pacientes tomaban medicamentos concomitantes.

En la segunda parte del estudio, la edad media era de 63,8 años, el 78 % eran varones y el 100 % tomaban medicamentos concomitantes.

Los pacientes que se sometieron a procedimientos de cateterización cardíaca de diagnóstico (parte 1 y parte 2) o de intervención (parte 2) fueron elegibles para la participación en el estudio. Los procedimientos cumplían con el estándar de atención en cada uno de los hospitales participantes, seguido del uso del FemoSeal™ VCS. Los datos de los pacientes se recogieron al inicio, durante el procedimiento, y transcurridos un día y 30 días después del procedimiento. Los resultados se resumen en la **tabla 1.5** e indican que FemoSeal™ VCS es seguro y eficaz para su uso en esta población de pacientes.

**Tabla 1.5 Resultados clínicos informados en un estudio previo a la comercialización**

|                                                                                                                       | Parte 1      | Parte 2                   |
|-----------------------------------------------------------------------------------------------------------------------|--------------|---------------------------|
| Número de pacientes                                                                                                   | 20           | 60                        |
| Tiempo medio hasta la hemostasia                                                                                      | 1,2 minutos  | 1,6 minutos <sup>a</sup>  |
| Tiempo medio hasta la deambulación                                                                                    | 72,2 minutos | 87,5 minutos <sup>b</sup> |
| Incidencia de complicaciones vasculares graves <sup>c</sup>                                                           | 0 (0 %)      | 1 (2 %)                   |
| Número de pacientes con efectos adversos                                                                              | 5 (25 %)     | 19 (32 %)                 |
| Fracaso del tratamiento (definida como complicaciones vasculares importantes, necesidad de compresión manual o ambas) | 0 (0 %)      | 3 (5 %)                   |
| Fallos en el funcionamiento del dispositivo                                                                           | 0 (0 %)      | 6 (10 %)                  |

<sup>a</sup> Basado en el tamaño total de la muestra de 58, porque dos pacientes no alcanzaron la hemostasia en el momento de la intervención debido a punciones ipsilaterales anteriores. La hemostasia se logró a los 7 minutos y 37 minutos para estos pacientes.

<sup>b</sup> Basado en el tamaño total de la muestra de 59: Un paciente no estaba incluido porque se le colocó el ventilador debido a un edema pulmonar y no pudo caminar durante más de una semana.

<sup>c</sup> Definido como complicación vascular que requiere transfusión de sangre o reparación quirúrgica, o infección local que requiere la administración de antibióticos, hospitalización o prolongación de la hospitalización o desbridamiento del sitio.

No se observaron complicaciones vasculares importantes en la parte 1 del estudio. Se notificó una complicación vascular grave en la parte 2 del estudio: pseudoaneurisma que se notificó en el plazo de un día tras la intervención. El acontecimiento requirió compresión guiada por ultrasonido y una inyección de trombina en el pseudoaneurisma y extendió la hospitalización del paciente.

De los cinco acontecimientos adversos notificados en la parte 1 del estudio, hubo un posible acontecimiento adverso relacionado con el dispositivo: un acontecimiento no grave de hemorragia rápida un día después del procedimiento. De los 19 acontecimientos adversos notificados en la parte 2 del estudio, se observaron tres acontecimientos adversos no graves relacionados con el dispositivo del hematoma, y se observaron seis posibles acontecimientos no

graves relacionados con el dispositivo, incluidos tres informes de exudado persistente, dos hematomas y dolor en una pierna después del ejercicio.

En la parte 2, tres pacientes fueron considerados fracasos del tratamiento: dos debido a la imposibilidad de lograr la hemostasia sin el uso de compresión y uno debido a la complicación vascular importante (pseudoaneurisma). No hubo fracasos del tratamiento en la parte 1 del estudio.

De los seis fallos de funcionamiento del dispositivo en la parte 2 del estudio, tres no interfirieron con el procedimiento, uno se atribuyó a un error del usuario, uno fue una fuga del introductor y otro fue una rotura de la unión del filamento. Los dos últimos problemas se abordaron con actualizaciones de modelos implementadas en C11202.

La parte 2 del estudio clínico previo a la comercialización no informó de los resultados del seguimiento de 6 meses debido al incumplimiento por parte de los pacientes. El estudio clínico previo a la comercialización (EU-SE-001) de 30 días, que coincide con el periodo de seguimiento de la bibliografía clínica, demuestra que FemoSeal™ VCS es seguro y eficaz.

### 1.4.2 Resumen de datos de estudios clínicos posteriores a la comercialización

En la **tabla 1.6** se describen cuatro estudios clínicos posteriores a la comercialización finalizados. Estas investigaciones clínicas no están publicada ni disponibles en línea.

**Tabla 1.6 Estudios clínicos posteriores a la comercialización**

| Estudios clínicos posteriores a la comercialización finalizados                                |              |                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                            |
|------------------------------------------------------------------------------------------------|--------------|--------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Nombre del estudio                                                                             | Año/IC       | Tipo de estudio                                                                      | Objetivos                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Hitos                                                                                                                                                                                                                                                                                                                                                                          | Criterios de aceptación potencial                                                                                                                          |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)<br>User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI | Estudio posterior a la comercialización, aceptabilidad del usuario de nuevos envases | Estudio posterior a la comercialización realizado en la actualización del modelo FemoSeal Vascular® Closure System n.º 11202 que tiene un sistema de distribución modificado en comparación con el primer modelo (n.º 11200) para documentar la funcionalidad.<br><br>El objetivo del estudio era obtener información sobre las instrucciones de uso revisadas, el proyecto de formación para médicos y enfermeros, confirmar las evaluaciones realizadas en el análisis de riesgos y proporcionar información | 100 pacientes <ul style="list-style-type: none"> <li>63 hombres / 37 mujeres</li> <li>Edad media de 68 años para mujeres, 65 años para hombres</li> </ul> 2 hospitales suecos, 6 médicos<br><br>112 dispositivos<br><br>Datos capturados en los formularios de registro de pacientes (CRF)<br><br>Tiempo de observación previsto: 30 minutos desde el momento de la aplicación | Resultados<br><br>1. Ilustraciones/instrucciones en las instrucciones de uso consideradas informativas y adecuadas<br><br>2. Hemostasia inmediata (91/100) |

|                                                                                   |                                                         |                                                          |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
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|                                                                                   |                                                         |                                                          | sobre cualquier mejora en la calidad de los productos.                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008) | Dr. Nicolas Moes, Innsbruck Medical University, Austria | Evaluación confirmatoria posterior a la comercialización | El objetivo de este estudio fue evaluar la seguridad y el rendimiento de FemoSeal® utilizado durante la rutina clínica normal en pacientes sometidos a cateterización cardiaca diagnóstica o a procedimiento intervencionista cardiaco percutáneo realizado con vaina de 7 F. | 50 pacientes consecutivos<br><br>Indicación: cateterismo cardiaco invasivo o diagnóstico desde la arteria femoral común<br><br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yr)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                              | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yr) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Criterios de valoración principales <ul style="list-style-type: none"><li>Criterio principal de valoración de la eficacia: TTH (tiempo hasta la hemostasia) con o sin exudado, pero sin compresión adicional, manual o mecánica.</li><li>Criterio de valoración de la seguridad: incidencia de acontecimientos adversos — complicaciones vasculares menores y mayores y todos los demás acontecimientos adversos— graves y no graves durante la duración del estudio (es decir, hasta el alta del paciente).</li></ul> Resultados <ul style="list-style-type: none"><li>Tiempo medio hasta la hemostasia</li><li>Diagnóstico - 56,6 ± 29 segundos</li><li>Intervencionista 59,9 ± 16,2 segundos</li><li>Todos los pacientes 57,8 ±26,3</li><li>Todos los pacientes pudieron deambular sin problemas tras 4 horas de reposo en cama.</li></ul> Resultados de seguridad <ul style="list-style-type: none"><li>49/50 (98 %) sin complicaciones vasculares hasta el alta hospitalaria</li><li>Tiempo medio para el alta: 2,6 días</li><li>1/50 (2 %) de hemorragia leve al día siguiente después de una deambulación irregular el día de la angiografía</li></ul> |
| n                                                                                 | 50                                                      |                                                          |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| men                                                                               | 35 (70%)                                                |                                                          |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| women                                                                             | 15 (30%)                                                |                                                          |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| PCI cases                                                                         | 15                                                      |                                                          |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| age (yr)                                                                          | 62.8±11.1                                               |                                                          |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| body mass index (kg/m²)                                                           | 25.4±6.7                                                |                                                          |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| systolic BP (mmHg)                                                                | 131.2±20.9                                              |                                                          |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| diastolic BP (mmHg)                                                               | 77.9±10.6                                               |                                                          |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| diabetes mellitus                                                                 | 9 (18%)                                                 |                                                          |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| arterial hypertension                                                             | 34 (68%)                                                |                                                          |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| previous coronary intervention                                                    | 13 (26%)                                                |                                                          |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| preprocedure aspirin                                                              | 50 (100%)                                               |                                                          |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| preprocedure clopidogrel                                                          | 50 (100%)                                               |                                                          |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Procedural unfractionated heparin                                                 | 15 (30%)                                                |                                                          |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Procedural abciximab                                                              | 2 (4%)                                                  |                                                          |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)    | RADI 2009                                               | Estudio posterior a la comercialización                  | El estudio debe informar si los clientes/usuarios percibieron algún problema con el nuevo paquete, especialmente en el lado                                                                                                                                                   | 25 dispositivos<br>4 hospitales suecos<br><br>16/25 (64 %) de los pacientes eran pacientes con ICP con                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Resultados1. Problemas relacionados con el envase: las aplicaciones 21/25 (84 %) tuvieron éxito; 4/25 (16 %) no tuvieron éxito (1: probando el |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |

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|----------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|--------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                        |                                         |                                                                                            | <p>exterior no estéril de la bolsa Tuvek/PET-PE.</p> <p>El estudio también debe proporcionar información sobre si el médico tratante percibe alguna diferencia en las etapas de aplicación/despliegue del dispositivo en comparación con los dispositivos utilizados previamente.</p> <p>El estudio también debe dar su opinión sobre cualquier necesidad adicional de mejora de la calidad del producto.</p> | <p>medicación anticoagulación intensiva</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                        | <p>nuevo introductor, 1 disco interior atravesó una arteriotomía en el paso de retroceso, el botón surgió y el disco exterior se colocó en el canal tisular de incisión, 2 no se logró la hemostasia inmediatamente a pesar de no haber tenido problemas de despliegue).</p> <p>2. Hemostasia inmediata 19/25 (76 %) pacientes</p> <p>3. Hemorragia 11/25 (44 %) - 9/25 (36 %) exudado/sangrado, 2/25 (8 %) hematomas</p> <p>Tasa total de eventos 19 %</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| <p>The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022)</p> | <p>2022/ Terumo Medical Corporation</p> | <p>Estudio prospectivo, multicéntrico, observacional y posterior a la comercialización</p> | <p>Demostrar aún más la seguridad y eficacia del FemoSeal™ VCS para lograr la hemostasia de los sitios de acceso de la arteria femoral común (CFA) en sujetos del mundo real sometidos a procedimientos endovasculares percutáneos</p>                                                                                                                                                                        | <ul style="list-style-type: none"> <li>• Seguimiento del paciente a los 30 días (<math>\pm 7</math> días) mediante visita hospitalaria o llamada telefónica.</li> <li>• Incorporación: De diciembre de 2021 a julio de 2022.</li> <li>• 230 sujetos incorporados que se someten a procedimientos endovasculares de diagnóstico o intervención en los que se utiliza el FemoSeal™.</li> </ul> <p>3 centros europeos: Francia (92 pacientes), Alemania (38 pacientes) y Bélgica (100 pacientes).</p> | <ul style="list-style-type: none"> <li>• <b>Datos demográficos/comorbilidades:</b> <ul style="list-style-type: none"> <li>- Sexo: 161 hombres (70 %) / 69 mujeres (30 %).</li> <li>- Edad media: <math>70 \pm 12</math>.</li> <li>- IMC: <math>26,1 \pm 4,95</math> kg/m<sup>2</sup>.</li> <li>- Hipertensión: 160 pacientes (69,6 %).</li> <li>- Dislipidemia: 128 (55,7 %).</li> <li>- Enfermedad arterial coronaria: 42 (18,3 %).</li> <li>- Fumador/a: 86 (37,6 %).</li> <li>- Exfumador/a: 66 (28,8 %).</li> <li>- Enfermedad coronaria: 34 (14 %).</li> <li>- Infarto de miocardio previo: 18 (7,8 %).</li> <li>- Revascularización de la arteria periférica: 12 (5,2 %) en la arteria carótida y 83 (37,5 %) en la arteria de las extremidades inferiores.</li> <li>- Tratamiento antiplaquetario (al inicio): 211 (91,7 %), incluidos 21 (9,1 %) de tratamiento antiplaquetario dual (DAPT).</li> </ul> </li> </ul> |

|  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|--|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <ul style="list-style-type: none"> <li>- Anticoagulación oral: 40 (17,4 %) pacientes.</li> <li>• <b>Características de intervención:</b> <ul style="list-style-type: none"> <li>- Entorno: 162 casos (70,4 %) de pacientes hospitalizados y 68 casos (29,6 %) de pacientes ambulatorios.</li> <li>- Indicación predominante: 147 casos (63,9 %) de claudicación.</li> <li>- Enfoque: 35 anterógrados (15,3 %) y 194 retrógrados (84,7 %).</li> </ul> </li> <li>• <b>Criterios de valoración principales:</b> <ul style="list-style-type: none"> <li>- El criterio de valoración combinado de seguridad (sin complicaciones graves de la extremidad del punto de acceso en las 6 horas posteriores al procedimiento) y eficacia (hemostasia satisfactoria del punto de punción) se logró en 215/226 (95,1 %) [IC del 95 %: 91,46; 97,55] pacientes en el conjunto de análisis completo y 215/230 (93,5 %) [IC del 95 %: 89,47; 96,30] en el conjunto tratado con FemoSeal™.</li> <li>- El criterio de valoración de la eficacia se alcanzó en 219/226 (96,9 %) IC [93,7; 98,7] de los pacientes.</li> <li>- El criterio de valoración de la seguridad se alcanzó en 220/230 (95,2 %) [IC del 95 %: 92,15; 97,90] pacientes.</li> </ul> </li> <li>• <b>Criterios de valoración secundarios:</b> <ul style="list-style-type: none"> <li>- Ausencia de complicaciones leves en el lugar de acceso durante seis horas después del procedimiento lograda en</li> </ul> </li> </ul> |
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|--|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <p>225/230 (97,8 %) [IC del 95 %: 95,00; 99,29].</p> <p>- Se logró la ausencia de complicaciones graves y leves en el lugar de acceso entre seis horas y 30 días después del procedimiento en 219/230 (95,2 %) [IC del 95 %: 91,60; 97,59] de los pacientes.</p> <p>- Tiempo medio hasta la hemostasia con el FemoSeal™ VCD: 0,42 (0,25; 0,50) minutos.</p> <p>- Tiempo medio hasta la deambulación: 5,00 (4,54; 5,50) minutos.</p> <p>- Duración media de la estancia hospitalaria: 23,98 (22,72; 25,00) horas.</p> <p>- Usabilidad del FemoSeal™ VCS: «fácil» o «muy fácil» de desplegar en el 98,7 % de los casos («fácil» de desplegar en 21 [9,2 %], «muy fácil» de desplegar en 205 [89,5 %]) con poca o ninguna resistencia al despliegue en 226 (98,3 %) de los casos.</p> <p>152/230 (66,1 %) de los pacientes tratados con la guía incluida en el kit FemoSeal™ (GW 0,038 in) y recomendada en el FemoSeal™ sin ninguna deficiencia del dispositivo ni acontecimientos adversos notificados.</p> |
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El estudio de 2006 se llevó a cabo para confirmar la seguridad y eficacia del dispositivo actual con un sistema de distribución mejorado y para obtener información sobre las instrucciones de uso y el programa de formación de FemoSeal™ VCS. El estudio incluyó a 100 pacientes y el criterio de valoración principal era si se logró la hemostasia o si se necesitaban compresiones manuales o mecánicas adicionales. Este estudio concluyó que la aplicación de FemoSeal™ VCS tuvo éxito en la mayoría de los casos (el 91 % logró hemostasia inmediata).

En el estudio de 2008 se incluyeron a 50 pacientes para evaluar la seguridad y el rendimiento del FemoSeal™ VCS cuando se utilizaba durante la rutina clínica normal en pacientes sometidos a cateterismo cardíaco con una vaina de 7 F. El criterio de valoración principal del estudio consistió en recopilar datos sobre el tiempo hasta la hemostasia y el tiempo hasta la deambulación sin compresión adicional, manual o mecánica. Los resultados del estudio concluyeron que el tiempo medio de hemostasia era de 57,8 segundos y que todos los pacientes deambulaban después de 4 horas de reposo en la cama.

El estudio de 2009 debía evaluar el nuevo envase del FemoSeal™ VCS. En el estudio participaron 25 pacientes. El criterio de valoración principal fue si el usuario experimentó algún problema con el envase. Los usuarios no notaron ningún problema con el nuevo envase del FemoSeal™ VCS. Este estudio también recopiló datos sobre el tiempo necesario para lograr la hemostasia.

El objetivo del estudio de 2022 es recopilar de manera proactiva datos de la seguridad y eficacia del FemoSeal VCS para lograr la hemostasia de los sitios de acceso de la arteria femoral común (CFA) en sujetos del mundo real sometidos a procedimientos endovasculares percutáneos. En el estudio participaron 230 pacientes. Los criterios de valoración principales para el registro son el éxito del procedimiento (es decir, la hemostasia correcta del punto de punción) y la reducción de complicaciones importantes (por ejemplo, lesión vascular, hemorragia relacionada con el lugar de acceso, infección del lugar de acceso, compresión manual repetida e isquemia aguda ipsilateral de la pierna relacionada con el nuevo lugar de acceso). El estudio concluyó que el FemoSeal™ VCS funciona bien en entornos reales y proporciona una hemostasia eficaz y bajas tasas de complicaciones en el lugar de acceso para pacientes sometidos a intervenciones endovasculares periféricas. Demuestra un buen rendimiento con un tiempo corto hasta la hemostasia y una buena respuesta de uso por parte del operador, lo que convierte al FemoSeal™ VCS en un dispositivo valioso para el cierre del acceso femoral.

### 1.4.3 Resumen de datos del seguimiento clínico posterior a la comercialización

#### 1.4.3.1 Seguimiento clínico posterior a la comercialización finalizado

En la **Tabla 1.7** se describe un resumen de las actividades de seguimiento clínico posteriores a la comercialización completadas.

**Tabla 1.7. Actividades de seguimiento clínico posterior a la comercialización**

| Actividades de seguimiento clínico posterior a la comercialización completadas |          |                                                   |                                          |                                                             |                                                                        |
|--------------------------------------------------------------------------------|----------|---------------------------------------------------|------------------------------------------|-------------------------------------------------------------|------------------------------------------------------------------------|
| Nombre de la actividad                                                         | Año/IC   | Tipo de estudio                                   | Objetivos                                | Hitos                                                       | Criterios de aceptación potencial                                      |
| 20210292 - FemoSeal Vascular                                                   | 2021 TMC | Encuesta clínica posterior a la comercialización: | Encuesta posterior a la comercialización | <ul style="list-style-type: none"> <li>120 casos</li> </ul> | 1-5 Evaluaciones de dispositivos a escala: afirmaciones de la encuesta |



| Actividades de seguimiento clínico posterior a la comercialización completadas |          |                                                                            |                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|--------------------------------------------------------------------------------|----------|----------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Closure System Clinical Survey Report (2021)                                   |          | encuesta de alta calidad                                                   | para recopilar comentarios prospectivos relacionados con el uso de FemoSeal™ Vascular Closure Device distribuido en los mercados de la Unión Europea.                                                                                                                                                                     | <ul style="list-style-type: none"> <li>8 médicos únicos con &gt;5 años de experiencia</li> <li>Varios países de Europa</li> </ul>                                                                                                                                                                                                           | <ul style="list-style-type: none"> <li>Criterios de aceptación <ul style="list-style-type: none"> <li>Las calificaciones 3-5 se consideran favorables</li> <li>Todas las afirmaciones deben tener ≥80 % de comentarios positivos</li> </ul> </li> <li>Resultados <ul style="list-style-type: none"> <li>Ninguna afirmación de la encuesta recibió &gt;20 % de respuestas desfavorables</li> <li>No se presentaron quejas contra el producto</li> </ul> </li> </ul>                           |
| 20210298 – 0.035” and 0038” Guidewire Clinical Survey Report (2021)            | 2021 TMC | Encuesta clínica posterior a la comercialización: encuesta de alta calidad | Encuesta posterior a la comercialización para recopilar comentarios prospectivos relacionados con el uso de la guía de 0,035” incluida con el 6Fr Angio-Seal™ VIP Vascular Closure Device (VCD) y de 0,038” incluida con el 8Fr Angio-Seal™ VIP VCD y el FemoSeal Vascular Closure System distribuidos en los mercados de | <ul style="list-style-type: none"> <li>Encuestas para la guía de 0,035” <ul style="list-style-type: none"> <li>106 encuestas</li> <li>64 médicos</li> </ul> </li> <li>Encuestas para la guía de 0,038” <ul style="list-style-type: none"> <li>109 encuestas</li> <li>55 médicos</li> </ul> </li> <li>12 encuestas retrospectivas</li> </ul> | <b>1-5 Evaluaciones de dispositivos a escala: afirmaciones de la encuesta</b> <ul style="list-style-type: none"> <li>Criterios de aceptación <ul style="list-style-type: none"> <li>Las calificaciones 3-5 se consideran favorables</li> <li>Todas las afirmaciones deben tener ≥80 % de comentarios positivos</li> </ul> </li> <li>Resultados <ul style="list-style-type: none"> <li>Todas las guías recibieron calificaciones aceptables</li> <li>No se presentaron</li> </ul> </li> </ul> |

| Actividades de seguimiento clínico posterior a la comercialización completadas                                                  |                         |                                                                            |                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|---------------------------------------------------------------------------------------------------------------------------------|-------------------------|----------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                 |                         |                                                                            | la Unión Europea.                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                | quejas contra el producto                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024<br><br>TMC/TE | Encuesta clínica posterior a la comercialización: encuesta de alta calidad | Recopilar comentarios prospectivos relacionados con el uso de FemoSeal VCS con guías distribuidos en el mercado de la UE. | <ul style="list-style-type: none"> <li>126 encuestas <ul style="list-style-type: none"> <li>7 centros</li> <li>5 países</li> </ul> </li> <li>14 de noviembre de 2023-11 de junio de 2024</li> <li>Especialidad médica: <ul style="list-style-type: none"> <li>Cirugía vascular</li> <li>Radiología intervencionista</li> <li>Angiología</li> </ul> </li> </ul> | <b>5 Evaluaciones de dispositivos a escala: afirmaciones de la encuesta</b> <ul style="list-style-type: none"> <li>Criterios de aceptación <ul style="list-style-type: none"> <li>Las calificaciones 3-5 se consideran favorables</li> <li>Todas las afirmaciones deben tener ≥80 % de comentarios positivos</li> <li>Si se producen acontecimientos adversos en esta encuesta, deben ser los previstos por la gestión de riesgos.</li> </ul> </li> <li>Datos demográficos de los pacientes <ul style="list-style-type: none"> <li>Mujer: 29,4 % (37/126)</li> <li>Hombre: 69,8 % (88/126)</li> <li>Sexo no revelado: 0,8 % (1/126)</li> <li>Edad &gt;75 años: 31,7 %</li> </ul> </li> <li>Resultados <ul style="list-style-type: none"> <li>Guía suministrada con FemoSeal™</li> </ul> </li> </ul> |

| Actividades de seguimiento clínico posterior a la comercialización completadas |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|--------------------------------------------------------------------------------|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                |  |  |  |  | <div> VCS: 101/126<br/> (80,2 %). </div> <div> <ul style="list-style-type: none"> <li>○ Duración del procedimiento (minutos): 63,4 (36,6) (media [DE]); 57,0 (36,0-81,0) (mediana [IQR])</li> <li>○ Todas las calificaciones de rendimiento de FemoSeal™ VCS fueron favorables.</li> <li>○ Todas las calificaciones de la guía suministrada con FemoSeal™ VCS fueron favorables.</li> <li>○ Un acontecimiento adverso (0,8 %): los discos de FemoSeal™ VCS no estaban bien alineados probablemente debido al uso de una guía rígida (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 pulgadas) que requirió compresión</li> </ul> </div> |

| Actividades de seguimiento clínico posterior a la comercialización completadas |  |  |  |  |                                   |
|--------------------------------------------------------------------------------|--|--|--|--|-----------------------------------|
|                                                                                |  |  |  |  | manual para lograr la hemostasia. |

Terumo Medical Corporation ha completado tres encuestas de alta calidad a los usuarios médicos durante el periodo de notificación actual (del 1 de septiembre de 2019 al 31 de agosto de 2024).

Los estudios clínicos de FemoSeal™ recopilaban datos clínicos proactivos en relación con la seguridad y el rendimiento del FemoSeal™ VCS durante el uso clínico. La encuesta incluyó preguntas centradas en el dispositivo general y los accesorios asociados, incluida la guía de 0,038 in y sus interacciones directas. Los estudios clínicos sobre la guía recopilaban datos clínicos proactivos en relación con la seguridad y el rendimiento durante el uso clínico de la guía de 0,038 in suministrada con el FemoSeal™ VCS. Las preguntas de la encuesta se centraron específicamente en el uso general de la guía, que va desde la inserción a través de la vaina del procedimiento en la vasculatura hasta la extracción de la guía.

El FemoSeal™ VCS y la guía de 0,038 in incluidos con el dispositivo recibieron todas las clasificaciones aceptables y se presentaron seis (6) reclamaciones por el dispositivo y nueve (9) no-reclamaciones por la guía basadas en la evaluación de los comentarios recibidos de los estudios clínicos de alta calidad. Las reclamaciones se han evaluado tanto para el FemoSeal como para la guía y se han evaluado como parte del proceso de seguimiento posterior a la comercialización de Terumo. No se identificaron nuevos riesgos ni niveles de riesgo.

Se completó una encuesta a los usuarios médicos en 2024 como parte de las actividades de PMCF. Los resultados de la encuesta demostraron que la calificación de rendimiento y la seguridad de FemoSeal™ VCS eran muy favorables en general. También se demostró la compatibilidad de otras guías distintas a la estándar suministrada con FemoSeal™ VCS.

#### 1.4.3.2 Seguimiento clínico posterior al lanzamiento en curso o previsto

TMC tiene una actividad de seguimiento clínico posterior a la comercialización en curso/planificada. Se realizará una encuesta clínica para recopilar prospectivamente información relacionada con el uso de la guía con FemoSeal VCS distribuida en el mercado de la UE. Los médicos completarán la encuesta para estudiar qué guías utilizaron durante el procedimiento. El objetivo de esta encuesta es abordar una brecha identificada como la falta de documentación y comentarios de revisores externos sobre la compatibilidad de FemoSeal™ VCS con el uso de otras guías de marcas ajenas a Terumo. La información incluye los resultados técnicos, el rendimiento clínico y la seguridad relacionados con el rendimiento del dispositivo con diferentes guías.

#### 1.4.4 Resumen de los datos de la revisión bibliográfica sistemática

Terumo Medical Corporation lleva a cabo revisiones sistemáticas de la bibliografía para recopilar y evaluar datos clínicos de seguridad y rendimiento a partir de estudios publicados sobre el FemoSeal™ VCS o dispositivos similares. El objetivo del análisis anual de la bibliografía publicada es identificar efectos secundarios desconocidos anteriormente, supervisar los efectos secundarios conocidos, identificar riesgos emergentes e identificar un posible uso indebido sistemático o un uso fuera de indicación del FemoSeal™ VCS.

La revisión bibliográfica sistemática más reciente, que cubrió el periodo desde el 1 de septiembre de 2019 hasta el 31 de agosto de 2024, identificó 29 estudios publicados que proporcionaron datos de seguridad clínica y rendimiento sobre FemoSeal™ VCS. Veintitrés referencias informaron del uso de FemoSeal™ VCS según las indicaciones y en nueve estudios se informó del uso no contemplado. En general, la revisión bibliográfica de los estudios específicos para el uso del FemoSeal™ VCS muestra una población en estudio que es representativa de los pacientes de la UE sometidos a procedimientos de cateterización vascular percutánea. Consulte la **sección 3** para obtener una lista de estas 23 publicaciones del uso según las indicaciones revisadas por expertos.

El rendimiento clínico se evaluó mediante las siguientes medidas:

- El tiempo hasta la hemostasia es mejor o comparable al estado de la técnica para el cierre percutáneo de la arteria femoral común.
- El tiempo hasta la deambulación es mejor o comparable la tecnología de vanguardia para el cierre percutáneo de la arteria femoral común.
- La tasa de complicaciones posoperatorias es comparable o inferior a la de los estándares de atención actuales.

Basándose en estas mediciones de rendimiento clínico, los datos de esta revisión bibliográfica demostraron que FemoSeal™ VCS se puede utilizar con éxito para cerrar la punción femoral (arteriotomía) en pacientes sometidos a cateterización percutánea utilizando una vaina de procedimiento de 7 F o menor. La hemostasia completa se logró en la mayoría de los pacientes (79,65-100 %) de los casos y se asoció con un tiempo medio hasta la hemostasia de 0,5 min, tiempo medio hasta el alta de 3 días. Entre el 69,2 y el 86,7 % de los pacientes pudieron deambular 5 h después del cierre, con una media de reposo posoperatorio en la cama de 349 min. Se observó un fallo de FemoSeal™ VCS en el 3,68-4 % de los casos y se necesitó compresión manual adicional en el 0,9-4,4 % de los procedimientos.

La seguridad clínica se evaluó mediante acontecimientos adversos que incluyen, entre otros:

- Sangrado
- Hematomas
- Pseudoaneurisma

- Moratón
- Fístula arteriovenosa
- Infección
- Muerte

Para cada uno de estos acontecimientos adversos, la tasa de incidencia informada para el FemoSeal™ VCS en los estudios incluidos fue inferior o comparable a las tasas informadas históricamente para la compresión manual y otros dispositivos de cierre vascular.

No se identificaron acontecimientos adversos mediante la revisión de 10 informes del caso, ya que no se identificaron riesgos nuevos, imprevistos, emergentes o inaceptables.

La eficacia general del uso de FemoSeal™ VCS durante la angiografía diagnóstica o las intervenciones quirúrgicas depende de múltiples factores, como el sexo, la edad, la anatomía del paciente, las comorbilidades, la colocación anatómica del punto de punción, la experiencia del cirujano, el método de despliegue del VCD, el cuidado posoperatorio, etc. Además del éxito técnico, incluido el logro de la hemostasia, FemoSeal™ VCS ofreció beneficios clínicos en relación con el cierre vascular después de la punción arterial femoral, como la reducción del tiempo hasta la hemostasia y la reducción del tiempo hasta la deambulación. Los resultados de rendimiento de FemoSeal™ VCS son coherentes con los esperados para este tipo de dispositivo cuando se usa según lo previsto. Algunas de las referencias recuperadas durante el periodo de búsqueda actual mostraron el uso del dispositivo en cuestión en una ubicación anatómica distinta de la arteria femoral común y para el cierre de arteriotomías >7 Fr, lo que se considera no contemplado.

Durante la revisión no se identificaron efectos secundarios desconocidos, riesgos emergentes ni un posible uso indebido sistemático del dispositivo. Sin embargo, si FemoSeal™ VCS lo utilizan médicos formados con cuidado, el producto sanitario funciona como un dispositivo clínico útil y necesario. En general, la terapia objetivo y, por lo tanto, FemoSeal™ VCS aborda la necesidad clínica que existe actualmente en el tratamiento de las complicaciones relacionadas con el acceso vascular.

En general, los datos de esta revisión bibliográfica no detectaron ningún problema de rendimiento o seguridad en el entorno clínico que se desconocía previamente, ni efectos adversos que se produjeron a tasas superiores a las previstas/aceptables. Por lo tanto, a partir de esta revisión bibliográfica se puede concluir que el FemoSeal™ VCS, cuando se utiliza para proporcionar compresión para la hemostasia en la arteriotomía después del cateterismo percutáneo, sigue funcionando como se esperaba y no está asociado con eventos de seguridad graves.

#### **1.4.5 Resumen de datos de vigilancia posteriores a la comercialización**

Existe un sistema de PMS proactivo y se completa una revisión de todas las quejas mensualmente y de conformidad con los procedimientos de fabricación internos. Se analizaron los datos de las quejas durante el periodo comprendido entre el 1 de septiembre de 2019 y el 31 de agosto de 2024. En total, se presentaron 28 informes de vigilancia de productos sanitarios

(MDV) y 476 informes de reclamaciones de clientes al fabricante. De los 28 informes de MDV, 27 estaban relacionados con eventos adversos y uno con mal funcionamiento del dispositivo. Se produjeron dos muertes durante el periodo de notificación, pero ninguna de las muertes notificadas se consideró relacionada con el dispositivo en cuestión. Entre las 476 quejas presentadas al fabricante, los motivos más comunes de las quejas fueron las dificultades de implementación (146 incidencias, tasa de incidencia del 0,0142 %). El modo de fallo de los eventos de extracción es el segundo más frecuente con una tasa del 0,0126 % (130 eventos).

FemoSeal Vascular Closure System tiene más de 1 030 136 de ventas en todo el mundo y 827 843 en el Espacio Económico Europeo. La frecuencia calculada de las reclamaciones basadas en las ventas globales es del 0,046 %. La tasa global de reclamaciones de los clientes es muy baja. No se identificaron nuevos riesgos que no estén incluidos en las instrucciones de uso y la documentación de riesgos.

Las tasas de incidencia de los efectos secundarios no deseados se muestran en la **tabla 1.2**. No se identificaron nuevos riesgos imprevistos, emergentes o inaceptables mediante las reclamaciones. No hubo aumentos significativos en la frecuencia o la gravedad de los efectos secundarios no deseados conocidos.

#### **1.4.6 Resumen general del rendimiento clínico y la seguridad**

El FemoSeal™ VCS está indicado para cerrar la punción femoral habitual (arteriotomía) en pacientes que se hayan sometido a cateterismo percutáneo con una vaina quirúrgica de 2,33 mm (7 F) o menor. Esta evaluación clínica se basa en un análisis exhaustivo de los datos clínicos y la bibliografía disponibles antes y después de la comercialización relevantes para el uso previsto del FemoSeal™ VCS.

Se llevó a cabo una revisión exhaustiva de la bibliografía publicada durante el periodo comprendido entre el 1 de septiembre de 2019 y el 31 de agosto de 2024. El conjunto de pruebas incluyó 29 estudios para el FemoSeal™ VCS. La evidencia proporcionada en la evaluación clínica concluye que, cuando se utiliza del modo indicado, el dispositivo en cuestión es seguro y eficaz y cualquier riesgo o efecto secundario no deseado, que pueda asociarse con el dispositivo en condiciones normales de uso, constituye riesgos aceptables cuando se ponderan frente a los beneficios para el paciente. Los resultados de rendimiento de los dispositivos en cuestión son coherentes con los esperados para este tipo de dispositivo cuando se usa según lo previsto.

Los posibles efectos secundarios no deseados asociados con el uso del FemoSeal™ VCS incluyen los acontecimientos adversos comúnmente notificados con medios alternativos de cierre de la arteriotomía, por ejemplo, hemorragia y hematoma. En general, las tasas de incidencia de los acontecimientos adversos notificados con el uso del FemoSeal™ VCS son similares a las tasas registradas con la compresión manual y dispositivos de cierre vascular similares.

Específicamente, en el caso de hemorragias y hematomas, las tasas registradas para FemoSeal™ VCS son inferiores a las tasas registradas para dispositivos de cierre vascular similares. Cada uno

de los eventos adversos notificados, tanto de la bibliografía publicada como de la vigilancia posterior a la comercialización, se habían identificado previamente (consulte la **sección 1.3**).

Los datos existentes sobre la seguridad clínica y el rendimiento de FemoSeal™ VCS sugieren que los beneficios para el paciente del uso de este dispositivo de cierre vascular superan los posibles riesgos cuando se utiliza de acuerdo con las instrucciones de uso.

Como se ha indicado en las secciones anteriores, los datos proporcionados para FemoSeal™ VCS demuestran la coincidencia entre los datos relacionados con el dispositivo en evaluación (p. ej., uso del dispositivo, resultados de seguridad, rendimiento clínico y beneficios clínicos), los dispositivos equivalentes identificados y los datos relacionados con dispositivos similares enumerados en la tecnología de vanguardia.

El análisis cruzado de los datos de seguridad no identificó ninguna laguna entre lo siguiente:

- Datos mencionados en la tecnología de vanguardia
- Datos específicos del dispositivo en evaluación
- Datos mencionados en los archivos de gestión de riesgos
- Los datos mencionados en el etiquetado y/o las instrucciones de uso (es decir, los riesgos residuales que se deben transmitir al usuario están abordados).

La seguridad clínica se ha demostrado por las bajas tasas de complicaciones identificadas en la bibliografía clínica revisada por pares publicada, los estudios clínicos promocionados por la empresa, la revisión de los datos posteriores a la comercialización y la ausencia de retiradas del mercado. No se han identificado problemas con el rendimiento, la bibliografía revisada contenía el uso de FemoSeal™ VCS que coincidía con el uso previsto del fabricante.

### **1.5 Posibles alternativas de diagnóstico o tratamiento**

La compresión manual se utiliza tradicionalmente para lograr la hemostasia en el lugar de la arteriotomía después de cateterismos vasculares. La compresión manual se ha asociado con la inmovilización del paciente durante largos periodos de tiempo (hasta 8 horas después de un procedimiento) y con molestias sustanciales y estancias hospitalarias prolongadas. Una revisión sistemática reciente reveló que la media de tiempo necesario para lograr la hemostasia con compresión manual era de 20,8 minutos.<sup>1</sup>

Las alternativas a la compresión manual incluyen dispositivos hemostáticos externos que aplican compresión mecánica al sitio de la arteriotomía. Estos dispositivos no acortan el tiempo de hemostasia o de deambulación, sino que reducen los requisitos del personal al sustituir la compresión manual por compresión mecánica. Los índices de acontecimientos adversos asociados al uso de la compresión mecánica son similares a los de la compresión manual.



Los dispositivos de cierre vascular, como FemoSeal™ VCS, están diseñados para cerrar la arteriotomía. Su objetivo es reducir el tiempo de hemostasia y permitir una deambulación más temprana. Una revisión sistemática reciente, que incluye 13 dispositivos disponibles comercialmente, halló que el tiempo medio para lograr la hemostasia con un dispositivo de cierre vascular era de 5,4 minutos. El tiempo medio de hemostasia para los dispositivos de cierre vascular individuales osciló entre 1 (FemoSeal™ VCS) y 14 minutos; la mayoría de los dispositivos es de entre 4 y 10 minutos.<sup>1</sup>

Entre los acontecimientos adversos notificados habitualmente asociados al cierre del lugar de la arteriotomía, con compresiones manuales, dispositivos hemostáticos externos o dispositivos de cierre vascular, se incluyen hematoma, sangrado en el lugar de acceso, pseudoaneurisma, fístula arteriovenosa e infección. La misma revisión sistemática (34 ensayos controlados aleatorizados, 14 401 pacientes) halló que las tasas de acontecimientos adversos eran similares entre la compresión manual y el uso de dispositivos de cierre vascular, con la excepción de que el sangrado tendía a ser un poco más alto con los dispositivos de cierre vascular.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R. y Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32-44.*

## 1.6 Perfil y formación sugeridos para los usuarios

Los usuarios previstos del FemoSeal™ Vascular Closure System son médicos con formación que les permite realizar el acceso arterial y el cierre para procedimientos endovasculares a través de la arteria femoral común y han participado en un programa de formación médica FemoSeal™ de Terumo Medical Corporation.

## 1.7 Normas armonizadas y comunes relevantes

| Referencia estándar | Año actual de cumplimiento/rev | Descripción                                                                                          |
|---------------------|--------------------------------|------------------------------------------------------------------------------------------------------|
| ISO 11070           | 2014/AMD1:2018                 | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                  |
| EN ISO 11070        | 2014/A1:2018                   | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                  |
| Guía de la FDA      | 20 de mayo de 2021             | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment |

| Referencia estándar | Año actual de cumplimiento/rev | Descripción                                                                                                                                                              |
|---------------------|--------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F2052          | 2015                           | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment                                 |
| ASTM F2213          | 2017                           | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment                                             |
| ASTM F2503          | 2020                           | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                                                           |
| ASTM F2182          | 2019                           | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging                                    |
| EN ISO 13485        | 2016/A11:2021                  | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 13485           | 2016                           | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 14644-1         | 2015                           | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1      | 2015                           | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2         | 2015                           | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2      | 2015                           | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3         | 2019                           | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |

| Referencia estándar        | Año actual de cumplimiento/rev | Descripción                                                                                                                                   |
|----------------------------|--------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 14644-3             | 2019                           | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                      |
| ISO 14698-1                | 2003                           | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                         |
| EN ISO 14698-1             | 2003                           | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                         |
| ISO 14698-2                | 2003/TC1:2004                  | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| EN ISO 14698-2             | 2003/TC 1:2004                 | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| USP <788>                  | N/A                            | PARTICULATE MATTER IN INJECTIONS                                                                                                              |
| Farmacopea de la UE 2.9.19 | N/A                            | Particulate Contamination: Sub-Visible Particles                                                                                              |
| IEC 62366-1                | 2015                           | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN 62366-1                 | 2015                           | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN ISO 14971               | 2019/A11:2021                  | Medical devices — Application of risk management to Medical devices                                                                           |
| ISO 14971                  | 2019                           | Medical devices — Application of risk management to Medical devices                                                                           |
| ASTM F1980                 | 2016                           | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                                           |
| EN ISO 10993-1             | 2020                           | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                    |

| Referencia estándar | Año actual de cumplimiento/rev | Descripción                                                                                                          |
|---------------------|--------------------------------|----------------------------------------------------------------------------------------------------------------------|
| ISO 10993-1         | 2018                           | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2      | 2006                           | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2         | 2006                           | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3      | 2014                           | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3         | 2014                           | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4      | 2017                           | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4         | 2017                           | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| EN ISO 10993-5      | 2009                           | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| ISO 10993-5         | 2009                           | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| EN ISO 10993-6      | 2016                           | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |
| ISO 10993-6         | 2016                           | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |
| EN ISO 10993-10     | 2023                           | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                       |
| ISO 10993-10        | 2021                           | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                       |
| EN ISO 10993-11     | 2018                           | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                      |

| Referencia estándar | Año actual de cumplimiento/rev | Descripción                                                                                                                                |
|---------------------|--------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-11        | 2017                           | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| EN ISO 10993-12     | 2021                           | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| ISO 10993-12        | 2021                           | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| EN ISO 10993-17     | 2009                           | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17        | 2002                           | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18        | 2020/A1:2022                   | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |
| EN ISO 10993-18     | 2020/A1:2022                   | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |
| EN ISO 10993-23     | 2021                           | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |
| ISO 10993-23        | 2021                           | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |
| ASTM F2382          | 2018                           | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)          |
| ASTM F756           | 2017                           | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                      |
| USP <85>            | N/A                            | [Bacterial Endotoxins Test. (Sterility)]                                                                                                   |

| Referencia estándar | Año actual de cumplimiento/rev | Descripción                                                                                                                                                                  |
|---------------------|--------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| USP <161>           | N/A                            | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72      | 2019                           | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135        | 2014/A1:2019                   | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135           | 2014/A1:2018                   | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7      | 2008/A1:2022                   | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |
| ISO 10993-7         | 2008/A1:2019                   | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                                            |
| EN 556-1            | 2024                           | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices              |
| EN ISO 11737-1      | 2018/A1:2021                   | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                                        |
| ISO 11737-1         | 2018/A1:2021                   | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                                        |
| EN ISO 11138-1      | 2017                           | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                                 |
| ISO 11138-1         | 2017                           | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                                 |

| Referencia estándar | Año actual de cumplimiento/rev | Descripción                                                                                                                              |
|---------------------|--------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 11138-2      | 2017                           | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| ISO 11138-2         | 2017                           | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| EN ISO 15223-1      | 2016                           | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| ISO 15223-1         | 2016                           | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| EN 1041             | 2008/A1:2013                   | Information supplied by the manufacturer of medical devices                                                                              |
| EN ISO 11607-1      | 2020/A1:2023                   | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| ISO 11607-1         | 2019/A1:2023                   | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| EN ISO 11607-2      | 2020/A1:2023                   | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes       |
| ISO 11607-2         | 2019/A1:2023                   | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes       |
| ASTM D4169          | 2016                           | Standard Practice for Performance Testing of Shipping Containers and Systems                                                             |
| ASTM F1886/F1886M   | 2016                           | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                      |

| Referencia estándar | Año actual de cumplimiento/rev | Descripción                                                                                                                                                                        |
|---------------------|--------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F2825          | 2018                           | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                           |
| ASTM F2096          | 2011 (R 2019)                  | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                                       |
| ASTM F88/F88M       | 2015                           | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                               |
| MDCG 2021-24        | 2021                           | Guidance on classification of medical devices                                                                                                                                      |
| MDCG 2020-3         | 2020                           | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD         |
| MDCG 2020-8         | 2020                           | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                                     |
| MDCG 2020-7         | 2020                           | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                                  |
| MDCG 2020-6         | 2020                           | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                               |
| MDCG 2019-9 v1      | 2022                           | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                           |
| MDCG 2019-8 v2      | 2020                           | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices |
| MDCG 2020-15        | 2020                           | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                           |
| MDCG 2021-11        | 2021                           | Guidance on Implant Card – ‘Device types’                                                                                                                                          |



| Referencia estándar | Año actual de cumplimiento/rev | Descripción                                                                                                                                                                                                                                                   |
|---------------------|--------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2021-19        | 2021                           | Guidance note integration of the UDI within an organisation's quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4      | 2021                           | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2         | 2019                           | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1         | 2019                           | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7         | 2018                           | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6         | 2018                           | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |
| MDCG 2018-4         | 2018                           | MDCG 2018-4 Annex: UDI database Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                                                                                                  |
| MDCG 2018-3 v1      | 2020                           | Guidance on UDI for systems and procedure packs                                                                                                                                                                                                               |
| MDCG 2021-25        | 2021                           | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC                                                                 |
| Meddev 2.12-2 Rev 2 | 2012                           | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                                                                                        |

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### 3.0 HISTORIAL DE REVISIONES

| Número de revisión<br>SSCP   | Fecha de<br>publicación | Descripción del cambio                                                                                            | Revisión validada por el<br>organismo notificado                                                                                                                                                                                                                                                                                                                                        |
|------------------------------|-------------------------|-------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022                 | 20 de enero de<br>2023  | Publicación inicial, tras<br>la certificación CE del<br>MDR                                                       | <p><input checked="" type="checkbox"/> Sí</p> <p>Idioma de validación:<br/>English</p> <p><input type="checkbox"/> No (solo aplicable a<br/>dispositivos implantables de<br/>clase IIa o algunos IIb (MDR,<br/>artículo 52 (4), 2.º párrafo) para<br/>los que el SSCP aún no está<br/>validado por el NB)</p> <p><input type="checkbox"/> Otra (especificar):</p>                       |
| SSCP-FS-2023 –<br>Revisión 1 | 15 de marzo de<br>2024  | Actualización para el<br>periodo comprendido<br>entre el 1 de enero de<br>2019 y el 31 de<br>diciembre de 2023    | <p><input checked="" type="checkbox"/> Sí</p> <p>Idioma de validación:<br/>English</p> <p><input type="checkbox"/> No (solo aplicable a<br/>dispositivos implantables de<br/>clase IIa o algunos IIb [MDR,<br/>artículo 52 {4}, 2.º párrafo]<br/>para los que el SSCP aún no<br/>está validado por el organismo<br/>notificado)</p> <p><input type="checkbox"/> Otra (especificar):</p> |
| SSCP-FS-2024<br>Revisión 1   |                         | Actualización para el<br>periodo comprendido<br>entre el 1 de septiembre<br>de 2019 y el 31 de<br>agosto de 2024. | <p><input type="checkbox"/> Sí</p> <p>Idioma de validación:<br/>English</p> <p><input type="checkbox"/> No (solo aplicable a<br/>dispositivos implantables de<br/>clase IIa o algunos IIb [MDR,<br/>artículo 52 {4}, 2.º párrafo]<br/>para los que el SSCP aún no<br/>está validado por el organismo<br/>notificado)</p> <p><input type="checkbox"/> Otra (especificar):</p>            |

|                            |               |                                                                  |                                                                                                                                                                                                                                                                                                                                                                                 |
|----------------------------|---------------|------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>Revisión 2 | June 20, 2025 | Revisado en función de las consultas del NSAI para su validación | <div><input checked="" type="checkbox"/> Sí</div> <div>Idioma de validación:<br/>English</div> <div><input type="checkbox"/> No (solo aplicable a dispositivos implantables de clase IIa o algunos IIb [MDR, artículo 52 {4}, 2.º párrafo] para los que el SSCP aún no está validado por el organismo notificado)</div> <div><input type="checkbox"/> Otra (especificar):</div> |
|----------------------------|---------------|------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

**Kokkuvõte ohutusest ja kliinilisest toimivusest****FemoSeal™ Vascular Closure System**

|                                         |                                                                                             |
|-----------------------------------------|---------------------------------------------------------------------------------------------|
| <b>Tootja</b>                           | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 USA         |
| <b>Tootja SRN</b>                       | US-MF-000019594                                                                             |
| <b>Juhtkonna esindaja / PRRC</b>        | Kimberly Feitl<br>Vice President, Quality                                                   |
| <b>Põhi-UDI-DI</b>                      | 38970FS79                                                                                   |
| <b>EMDN-number</b>                      | C900199 – hemostaasisüsteemid – muu                                                         |
| <b>Seadmeklass</b>                      | III klass                                                                                   |
| <b>Esimese CE-märgise saamise aasta</b> | 2005                                                                                        |
| <b>Esindaja Euroopa Liidus</b>          | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgia<br>SRN: BE-AR-000001433 |
| <b>Teavitatud asutus:</b>               | NSAI<br>CE 0050                                                                             |

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Ohutuse ja kliinilise toimivuse kokkuvõtte (SSCP) eesmärk on anda avalikkusele ligipääs FemoSeal™ Vascular Closure Systemi (VSC) ohutuse ja kliinilise toimivuse peamiste aspektide uuendatud kokkuvõttele.

Kokkuvõtte seadme ohutusest ja kliinilisest toimivusest kasutajatele/tervishoiutöötajatele on esitatud **lõigus 1.0**.

## **1.0 KOKKUVÕTE KASUTAJATELE/TERVISHOIUTÖÖTAJATELE**

SSCP ei asenda kasutusjuhendit, mis on seadme ohutu kasutamise tagamise põhidokument, ega anna ettenähtud kasutajatele või patsientidele diagnoosimise või ravi soovitusi. SSCP ei asenda kohustuslikku teavet implantaadikaartidel ega muudes kohustuslikes dokumentides.

### **1.1 Seadme kavandatud sihtotstarve**

#### **1.1.1 Ettenähtud kasutus**

FemoSeal™ Vascular Closure System on meditsiiniseade, mis on ette nähtud arteri punktsioonikoha sulgemiseks pärast perkutaanset kateteriseerimist läbi ühisreiarteri.

#### **1.1.2 Kasutusnäidustused**

FemoSeal™ Vascular Closure System on ette nähtud kasutamiseks ühisreiarteri punktsioonikoha (arteriotoomia) sulgemiseks patsientidel, kellele on tehtud perkutaanne kateteriseerimine 7 Fr (2,33 mm) või väiksema protseduurikanüüliga.

#### **1.1.3 Vastunäidustused ja/või piirangud**

FemoSeal™ Vascular Closure Systemi kasutamine on vastunäidustatud patsientidel, kelle arteriotoomias kasutati kanüüle ja seadmeid, mis olid suuremaid kui 7 Fr (2,33 mm).

#### **1.1.4 Patsientide sihtrühmad**

FemoSeal™ Vascular Closure Systemi ohutus ja efektiivsus on tõestatud 18-aastastel ja vanematel patsientidel, kes on läbinud perkutaanse kateteriseerimise, kus kasutati 7 Fr (2,33 mm) või väiksemat protseduurikanüüli.

#### **1.1.5 Patsientide erirühmad**

FemoSeal™ Vascular Closure Systemi ohutus ja efektiivsus ei ole tõestatud järgmistel patsiendirühmadel.

- Olemasoleva autoimmuunhaigusega patsiendid.
- Terapeutilist trombolüüsi saavad patsiendid.
- Kliiniliselt olulise perifeersete veresoonte haigusega patsiendid.
- Ravimata hüpertensiooniga patsiendid ( $> 220$  mmHg süstoolne või  $> 110$  mmHg diastoolne).
- Veritsushäiretega patsiendid, sh trombotsütoopenia (trombotsüütide arv  $< 100\,000$ ) või aneemia (Hgb  $< 10$  mg/dl).
- Patsiendid, kelle ühisreiarteri valendik on väiksem kui 5 mm.

- Neeru- ja/või maksakahjustusega patsiendid.
- Muu asjakohase kaasuva haigusega patsiendid.
- Spetsiifilise rassilise ja/või etnilise päritoluga patsiendid.
- Patsiendid, kellel oli 72 tunni jooksul müokardiinfarkt.
- Patsiendid, kellel on punktsioonikohas veresoonesiirik või stent.
- Rasedad või imetavad patsiendid.
- Alla 18-aastased patsiendid.

### 1.1.6 Ettenähtud kasutajad

FemoSeal™ Vascular Closure Systemi ettenähtud kasutajad on arstid, kes on saanud väljaõppe arteriaalse ligipääsu ja sulgemisega endovaskulaarseteks protseduurideks ühisreiarteri kaudu ning kes on osalenud Terumo Medical Corporationi FemoSeal™-i arstide väljaõppeprogrammis.

## 1.2 Seadme kirjeldus

### 1.2.1 Seadme kirjeldus

FemoSeal™ Vascular Closure System, mida toodab Terumo Medical Corporation (TMC), on resorbeeruv vaskulaarne sulgemisseade, mis on kavandatud reiarteri hemostaasi saavutamiseks pärast perkutaanset kateteriseerimist ühisreiarteri kaudu.

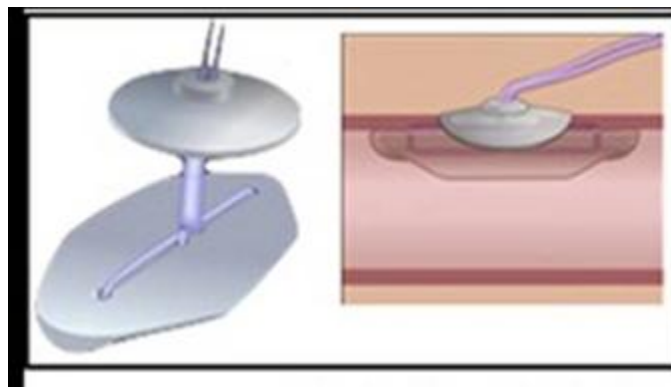
FemoSeal™-i sulgemiselemendid koosnevad kahest resorbeeruvast polümeerkettast, sisemisest sulgurist ja välimisest lukustusplaadist, mida hoiab koos resorbeeruv multifilament, mis koos sulgevad arteriotoomia mehhaaniliselt (vt **joonis 1.1** ja **joonis 1.2**). Pärast korpuse koonilisest kanüülist väljutamist pressitakse välimine lukustusplaat mööda multifilamendist telge alla, tekitades sisemise sulguri ja välimise lukustusplaadi vahel punktsioonikoha mehaanilise sulguse. Sisemist sulgurit ja välimist lukustusplaati hoiab multifilamendist teljel paigal hõordejõud. Hemostaas saavutatakse mehaaniliste vahenditega. Sulgemiselemendid lagunevad hüdroolüüsi teel.

Implanteeritavad sulgemiskomponendid, sisemine sulgur ja välimine lukustusplaat lagunevad kaheksateistkümne (18) kuuga, multifilament laguneb ja resorbeerub hüdroolüüsi teel ümbritsevasse kudedesse hinnanguliselt kahe (2) kuni kolme (3) aastaga. Implanteeritavate sulgemiskomponentide võimet säilitada arteriotoomial kompressiooni on katsetatud kuni kaheksa (8) tunni vältel. Laguproduktid metaboliseeruvad ja erituvad uriiniga või hingatakse süsinikdioksiidi kujul välja kopsude kaudu. Loomkatsetes ei ole täheldatud akumulatsiooniefekti. FemoSeal™-i komponendid, mis puutuvad protseduuri ajal kokku eluskudede või verega, on korpuse kooniline kanüül, dilataator, tihendustoru, tõukur ja juhtetraat.

**Joonis 1.1 Sisemine sulgur ja välimine lukustusplaat**

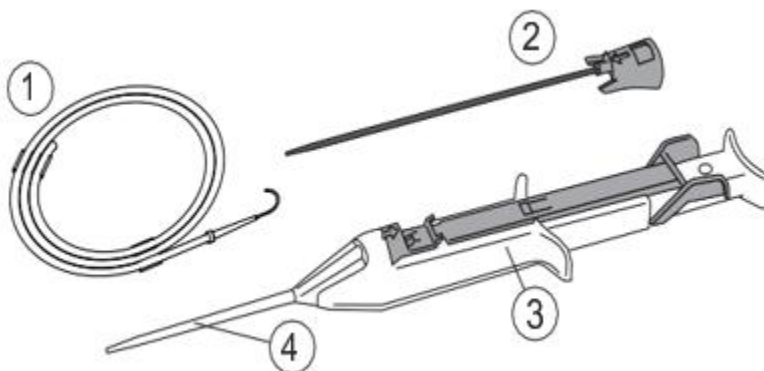


**Joonis 1.2 Sisemine sulgur ja välimine lukustusplaat paigaldatuna**



FemoSeal™-i seade on pakendatud koos dilataatori ja 0,038-tollise (0,97 mm) läbimõõduga, 27,5-tollise (70 cm) pikkuse juhtetraadi ja J-sirgendajaga, vt **joonis 1.3** allpool. Juhtetraat asub polüetüleentorus. Kõik osad on pakitud kinnisele paberalusele. Pakend sisaldab ka patsiendi implantaadikaarti. FemoSeal™ Vascular Closure System ei vaja seadme sihtotstarbeliseks tööks lisatarvikuid ning seade on mõeldud kasutamiseks ainult koos dilataatori ja juhtetraadiga, mis on kaasas toote pakendis.

**Joonis 1.3 FemoSeal™ VCS-i seade koos juhtetraadi ja dilataatoriga**



## 1.2.2 Toormaterjalid ja komponendid

Allolevas tabelis 1.1 on loetletud FemoSeal™ VCS-i komponendid.

**Tabel 1.1 FemoSeal™ VCS-i toormaterjalid ja komponendid**

| Osa number | Kirjeldus                                                   |                                                           | Materjalid                                                                                                                                                                                   |
|------------|-------------------------------------------------------------|-----------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1          | 0,038" (0,97 mm) juhtetraat koos juhtetraadi J-sirgendajaga |                                                           | Juhtetraat: roostevaba teras 304<br>J-sirgendaja: polüpropüleen, valge pigment<br>Klamber: polüetüleen<br>Torud: polüetüleen                                                                 |
| 2          | FemoSeali dilataator                                        |                                                           | Muhv: tetraahüdrofuraan, sinine pigment, polübutüleenereftalaat (PBT)<br><br>Toru: suure tihedusega polüetüleen (HDPE), must pigment<br><br>Libiaine: Silikoon Dow Corning 360               |
| 3/4        | FemoSeali seade                                             | Vormitud RD7 – sisemine sulgur ja välimine lukustusplaat* | Glükoliidi, trimetüleenkarbonaadi ja ε-kaprolaktooni kopolümeer ning trimetüülpropan (TMP, initsiaator)                                                                                      |
|            |                                                             | Multifilament*                                            | L,L-laktiidi, trimetüleenkarbonaadi ja ε-kaprolaktooni segmenteeritud kopolümeer ning 1,3-propaandiool (initsiaator)<br><br>Pinnakate on glükoliidi, ε-kaprolaktooni ja L-lüsiini kopolümeer |
|            |                                                             | Tihendustoru                                              | Polüpropüleen                                                                                                                                                                                |
|            |                                                             | Tõukur                                                    | 304V roostevaba teras                                                                                                                                                                        |
|            |                                                             | Liugnupp                                                  | Polübutüleenereftalaat (PBT)                                                                                                                                                                 |
|            |                                                             | Korpus                                                    | Polübutüleenereftalaat (PBT)                                                                                                                                                                 |
|            |                                                             | Nupp                                                      | Polübutüleenereftalaat (PBT)                                                                                                                                                                 |
|            |                                                             | Nupu kork                                                 | Polüoksümetüleen (POM)/polüatsetaalkopolümeer                                                                                                                                                |
|            |                                                             | Hülss                                                     | Polübutüleenereftalaat (PBT)                                                                                                                                                                 |
|            |                                                             | Seib                                                      | Polübutüleenereftalaat (PBT)                                                                                                                                                                 |
|            |                                                             | Koonus                                                    | Polüpropüleen                                                                                                                                                                                |

|  |  |                             |                                                           |
|--|--|-----------------------------|-----------------------------------------------------------|
|  |  | Korpuse kork                | Polübutüleenereftalaat (PBT)                              |
|  |  | Turvalukk                   | Polübutüleenereftalaat (PBT),<br>sinine pigment           |
|  |  | Hülsi kork                  | Polübutüleenereftalaat (PBT)                              |
|  |  | Toru tihend                 | Silikoon Shore 70 A                                       |
|  |  | Korpuse tihend              | Silikoon Shore A 50                                       |
|  |  | Vedru                       | 302 roostevaba teras                                      |
|  |  | Korpuse kooniline<br>kanüül | Polüpropüleen<br><br>Silikoon Dow Corning 360,<br>heksaan |

\* Seadme implanteeritav osa; implanteeritavad komponendid on MRT-ohutud

FemoSeal™ VCS on steriliseeritud etüleenoksiidiga (EO) ja see on ühekordselt kasutatav meditsiiniseade. FemoSeal™ VCS-i seade on välja töötatud selliselt, et seda ei saa korduvalt kasutada.

### **Toimimisviis**

FemoSeal™ VCS võimaldab saavutada mehaanilise hemostaasi implanteeritavate sulgemiselementide paigaldamisega ühisreiearterisse ja sellest väljapoole. Verejooksu tõkestava mehhanismi tekitavad sisemine sulgur, mis sulgeb punktsioonikoha, ja välimine lukustusplaat, mis hoiab sisemist sulgurit paigal.

### **1.2.3 Kliiniline kasu**

FemoSeal™ VCS-i kasutamine pakub pärast ühisreiearteri punktsiooni järgmisi kliinilisi eeliseid.

- Lüheneb hemostaasiks kuluv aeg<sup>1</sup>
- Lüheneb liikuma hakkamiseni kuluv aeg<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

### **1.2.4 Varasemad põlvkonnad või variandid**

- FemoSeal™ VCS-i esimest versiooni (nr 11200) müüdi Euroopa turul 2005. aastal ja osaliselt ka 2006. aastal.
- Praegune FemoSeal™ VCS (nr 11202), millel on täiustatud paigaldussüsteem, on olnud turul alates 28. märtsist 2006.

### 1.2.5 Seadmega koos kasutatavad lisatarvikud

FemoSeal™-i seade on pakendatud koos dilataatori ja 0,038-tollise (0,97°mm) läbimõõduga, 27,5-tollise (70°cm) pikkusega juhtetraadi ja J-sirgendajaga. Juhtetraat on FemoSeal™-i seadme lisatarvik. J-sirgendaja on juhtetraadi osa, dilataator on FemoSeal™-i seadme osa. Juhtetraat on ainus vajaminev lisatarvik. Juhtetraat asub polüetüleentorus. Kõik osad on pakitud kinnisele paberalusele. Pakend sisaldab ka patsiendi implantaadikaarti. FemoSeal™ Vascular Closure System ei vaja seadme sihtotstarbeliseks tööks lisatarvikuid ning seade on mõeldud kasutamiseks ainult koos dilataatori ja juhtetraadiga, mis on kaasas toote pakendis.

### 1.2.6 Muude seadmega koos kasutamiseks ette nähtud seadmete ja toodete kirjeldus

FemoSeal™ VCS ei vaja ettenähtud viisil toimimiseks lisaseadmeid.

## 1.3 Riskid ja hoiatused

### 1.3.1 Jääkriskid ja soovimatud mõjud

Teadaolevad või eeldatavad kõrvalnähud, kahjustused ja tüsistused, mis on seotud jääkriskidega FemoSeal™ VCS-i kasutamise tõttu, on loetletud **tabelis 1.2**. Juhtude esinemismäär põhineb riskidokumentatsiooni analüüsil ja arvutati turustamisjärgse järelevalve andmete põhjal ajavahemikust 1. septembrist 2019 kuni 31. augustini 2024. FemoSeal™ VCS-iga ei ole teadaolevaid jääkriske ning kõiki kohaldatavaid riske on käsitletud kasutusjuhendis ja riskijuhtimisprotsessis.

**Tabel 1.2. FemoSeali kõrvalnähud/tüsistused**

| Kahju                  | Esinemissagedus (%) | Leevendavad tegurid                                                                                                                                       |
|------------------------|---------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
| Allergiline reaktsioon | 0,0000              | Toote disainis, tootmisjuhistes, toote märgistuses ja arstide väljaõppes on rakendatud tegevusi ja kavasid, mille eesmärk on riski võimalikult vähendada. |
| Aneurüsm               | 0,0000              |                                                                                                                                                           |
| Arteriovenoosne fistul | 0,0001              |                                                                                                                                                           |
| Verekaotus/veritsus    | 0,0280              |                                                                                                                                                           |
| Surm                   | 0,0002              |                                                                                                                                                           |
| Ekhümoos               | 0,0000              |                                                                                                                                                           |
| Emboolia               | 0,0000              |                                                                                                                                                           |
| Võõrkehareaktsioon     | 0,0000              |                                                                                                                                                           |



| Kahju                                       | Esinemissagedus (%) | Leevendavad tegurid |
|---------------------------------------------|---------------------|---------------------|
| Hematoom                                    | 0,0027              |                     |
| Hemorraagia                                 | 0,0001              |                     |
| Infektsioon                                 | 0,0002              |                     |
| Põletikureaktsioon                          | 0,0000              |                     |
| Tuimus                                      | 0,0000              |                     |
| Valu                                        | 0,0000              |                     |
| Ebamugavustunne patsiendil                  | 0,0004              |                     |
| Protseduuri viivitus                        | 0,0065              |                     |
| Pseudoaneurüsm                              | 0,0004              |                     |
| Retroperitoneaalne veritsus                 | 0,0002              |                     |
| Sepsis                                      | 0,0000              |                     |
| Trombembolia                                | 0,0000              |                     |
| Tromboos                                    | 0,0001              |                     |
| Veresoone oklusioon / alajäseme isheemia    | 0,0002              |                     |
| Veresoone perforatsioon                     | 0,0000              |                     |
| Veresoone kudede dissektsioon/latseratsioon | 0,0003              |                     |

### 1.3.2 Hoiatused ja ettevaatusabinõud

#### Hoiatused

- Ärge kasutage, kui pakend on kahjustatud või kui steriilsusbarjääri on rikutud.
- Ärge kasutage pärast kõlblikkusaja lõppu, kuna biolagunevad komponendid ei pruugi piisavalt hästi toimida.
- Ärge kasutage, kui mõni ese on mingil viisil kahjustatud või defektne.
- FemoSeal™ Vascular Closure Systemi kasutamine olukorras, kus protseduurikanüül või ümbritsev kude võib olla bakteriaalselt saastunud, võib põhjustada infektsiooni.
- Kui kahtlustate tagumise arteriseina punktsiooni või mitut arteripunktsiooni, siis ärge tuginege arteriaalse hemostaasi saavutamiseks üksnes FemoSeal™ Vascular Closure Systemile. Kasutage manuaalset või mehaanilist lisakompressiooni.

6. Kui punktsioonikoht asub reiearteri bifurkatsioonil või sellest distaalsel, ei tohi FemoSeal™ Vascular Closure Systemit kasutada, sest see võib põhjustada sisemise sulguri valepaigutust. See võib põhjustada veritsustüsistusi ja/või normaalse verevoolu häireid.
7. Kui sisselõike kohas on püsiv arteriaalne verejooks, siis ärge lõigake multifilamenti enne, kui on saavutatud hemostaas. Kui hemostaasi ei saavutata, kinnitage multifilament steriilse haavaplaastriga ja avaldage kuni hemostaasi saavutamiseni lisasurvet. Püsiva arteriaalse verejooksu korral võivad tekkida tõsised veritsustüsistused, mis võivad lõppeda patsiendi tervisekahjustuse või surmaga.
8. Ärge kasutage FemoSeal™ Vascular Closure Systemit, kui punktsioonikoht on kubemesidemest proksimaalsel, sest see võib põhjustada retroperitoneaalse hematoomi.
9. Suurema verejooksuriskiga patsientidel võib tekkida suurem verekaotus, mis nõuab vereülekannet.
10. Kui sisemine ketas tuleb lahti, võib see põhjustada tromboosi ja/või embooliat.

#### **Ettevaatusabinõud**

1. FemoSeal™ Vascular Closure Systemi paigaldamise protseduuri peavad tegema arstid, kes on saanud seadme kasutamiseks piisava väljaõppe.
2. Enne FemoSeal™ Vascular Closure Systemi paigaldamist tehke piiratud reieangiogramm või ultraheliga juhitud reiepunktsioon.
3. Katkestage protseduur, kui:
  - ühisreiearteri valendiku läbimõõt on  $< 5$  mm;
  - ühisreiearteri punktsioonikoha läheduses on stenoos ja/või märkimisväärne naastulisus;
  - arteri punktsioonikoht asub reiearteri bifurkatsioonil või sellest distaalsel;
  - ühisreiearteri punktsioonikoha läheduses on anomaalsed sooneharud või sooneanomaaliad.
4. Hematoomi korral peab korpuse koonilise kanüüli arterisse sisestamisel olema eriti hoolikas.
5. Kasutage ühe seina punktsiooni tehnikat. Arteri tagaseina mitte punkteerida.
6. FemoSeal™ Vascular Closure Systemi kasutamisel tuleb alati järgida steriilset tehnikat.
7. FemoSeal™ Vascular Closure System on mõeldud ainult ühekordseks kasutamiseks ja seda ei tohi mingil viisil uuesti kasutada ega resteriliseerida. Seade FemoSeal™ on välja töötatud selliselt, et seda ei saa korduvalt kasutada.

8. Kui sisemise sulguri vabastamisel tekib ootamatu takistus, katkestage protseduur.
9. Sisemise sulguri õigeks paigaldamiseks paigutage oma põial nii, et nupp saaks vabalt tagasi hüpata.
10. Enne välimise lukustusplaadi paigaldamist veenduge, et FemoSeal™-i seadme korpuse koonilise kanüüli ots oleks nahapinna all. Kui patsendil on reiearteri ja naha vahel vähe ruumi, siis võib välimine lukustusplaat kogemata vabaneda naha peal.
11. Õigeks paigaldamiseks võib enne paigaldamist olla vajalik teha nahalõige.
12. Kui sisemine sulgur on arteri sees, kuid nuppu ei ole võimalik lõpuni alla vajutada ja välimist lukustusplaati paigaldada, võib olla vajalik operatsioon FemoSeal™-i sulgemiselementide eemaldamiseks.
13. Kui 18 kuu jooksul osutub vajalikuks sama reiearteri punktsioon, tuleb uus punktsioon teha vähemalt üks sentimeeter varasemast FemoSeal™ Vascular Closure Systemi paikmest proksimaalsele.
14. Andke patsiendile juhised, et ta järgiks sulgemiskoha ülevaatuse osas arsti suuniseid.
15. Andke patsiendile juhised, et ta kannaks patsiendikaarti järgmised 18°kuud endaga kaasas.

### **Ettevaatusabinõud väljakirjutamisel**

Enne väljakirjutamise kaalumist tuleb patsiendi seisundit hinnata järgmiste kliiniliste seisundite suhtes.

1. Veritsus ja/või hematoom sulgemiskohas.
2. Valu kõndimise ajal.
3. Infektsioonitunnused sulgemiskohas.

### **1.3.3 Valdkonna ohutuse parandusmeetmed**

Vahemikus 1. septembrist 2019 kuni 31. augustini 2024 anti teada ühest FemoSeal™ VCS-iga seotud valdkonna ohutuse parandusmeetmest.

2022. aastal kutsus Terumo vabatahtlikult tagasi FemoSeal™ VCS-i kaebuste tõttu, milles väideti, et Elktoni toodetud FemoSeali toote survejõu mõõtmise ja tagasitõmbeljõu katsetamise protsessis ja partiide vabastamisel esines tõrkeid. Lõuna-Koreast kutsuti tagasi kokku 950 seadet.

## 1.4 Kliiniline hindamine ja turustamisjärgne kliiniline järelkontroll

**Tabel 1.3** sisaldab loendit olulisematest uuringutest enne FemoSeal™ VCS-i turuletoomist ning turustamisjärgsetest uuringutest ja turustamisjärgse kliinilise järelkontrolli toimingutest. Tabelis on nimetatud ka uuringus kasutatud seadme versioon. FemoSeal™ VCS-i esimene versioon (nr 11200) oli turul kuni 2006. aastani, järgmine versioon (nr C11202) tuli turule 2006. aastal ja seda turustatakse ka praegu.

**Tabel 1.3 Olulisemate uuringute kokkuvõte**

| Turustamiseelsed funktsionaalsed loomkatsed                                                                                                                                                                                                                             | Seadme versioon            |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculture System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France).  | 11200                      |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                      |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                      |
| <b>Esimene kliiniline uuring inimesel</b>                                                                                                                                                                                                                               |                            |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                      |
| <b>Lõpetatud turustamisjärgsed kliinilised uuringud</b>                                                                                                                                                                                                                 |                            |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                                                                              | C11202<br>(praegune seade) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                                                                                       | C11202<br>(praegune seade) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                                                                                                                                                          | C11202<br>(praegune seade) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)                                                                                                                                                  | C11202<br>(praegune seade) |
| <b>Plaanitavad/käimasolevad turustamisjärgsed kliinilised uuringud</b>                                                                                                                                                                                                  |                            |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                                                                                                                                                              | C11202<br>(praegune seade) |
| <b>Turustamisjärgse kliinilise järelkontrolli toimingud</b>                                                                                                                                                                                                             |                            |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                                                                                                                                                               | C11202<br>(praegune seade) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                                                                                                                                                                      | C11202<br>(praegune seade) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024)                                                                                                                                         | C11202<br>(praegune seade) |

### 1.4.1 Turustamiseelsete loomkatsete ja kliiniliste uuringute kokkuvõte

**Tabelis 1.4** on kirjeldatud kõiki turustamiseelseid uuringuid, nii loomkatseid kui ka kliinilisi uuringuid.

**Tabel 1.4 Turustamiseelsete uuringute kokkuvõte**

| Turustamiseelsed funktsionaalsed loomkatsed                                                                                                                                                                                                                             |                                                                        |                              |                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Uuringu nimetus                                                                                                                                                                                                                                                         | Aasta/asutus                                                           | Uuringu tüüp                 | Eesmärgid                                                                                                                                                                                                      | Põhitulemused                                                                                                                                                                                                                                                                                          | Võimalikud aktsepteerimiskriteeriumid                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 2000<br>Radi Medical System AB<br><br>Teostanud Biomatech, Prantsusmaa | Loomkatse; uurimuslik uuring | Uuringu eesmärk oli hinnata veresoonkonnas hemostaasi saavutamiseks ette nähtud biolaguneva implantaadi biosobivust ja biofunktsionaalsust. Uuringus kasutati varuloomi uuringust nr 862 (dokument nr 1051-01) | N = 3 täiskasvanud utte, 1 loom ajapunkti kohta<br><br>Histopatoloogilise analüüsi, makroskoopilise hindamise ja ultrastruktuuraalse analüüsi järelkontroll<br><br>• 12 kuud<br>• 15 kuud<br>• 18 kuud<br><br>Värvidoppler-ultraheliga järelkontroll – 30 päeva une- ja reiearteri punktsioonikohtades | Arteri avatus<br>• Paigaldusjärgse verevoolu hindamine – 2/3 protseduuriga seotud verevoolu vähenemisest seondus ajutise arteriaalse vasospasmiga, mõlemad esinesid vasakus ühisunearteris.<br>• Värvidoppler-ultraheliuuring (4 nädalat) – 3/3 (100%) ilma suurema verevoolu vähenemiseta 30 päeva pärast implanteerimist<br><br>Makroskoopilised vaatlused<br>• 12 kuud – avatus kinnitatud makroskoopiliselt, puudub anatoomiliselt nähtav oklusioon; ei esine makroskoopilisi lokaalseid talumatuskahjustusi (hemorraagia, nekroos või neovaskularisatsioon); sisemise ketta kapseldumine märgatav<br>• 15 kuud – makroskoopiline vaatlus ei näidanud põletiku tunnuseid, ei tuvastatud sisemiste või välimiste ketaste jääke; välimise ketta piirkonnas paiknevad kapseldunud koed näisid samasugused kui 12 kuu vaatlusel<br>• 18 kuud – makroskoopiline vaatlus ei näidanud lokaalseid talumatuse tunnuseid, 3/3 välimine ketta nähtav, sisemise ketta lagunemine täielik; 1/3 (vasak ühisunearter) – |

|                                                                                                                                                                                                                                                                                |                                                                            |                                     |                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|-------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                                                                                                |                                                                            |                                     |                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                    | <p>implanteerimiskohas täheldatav arteriseina lohk (võib olla seotud seadme paigaldamisega)</p> <p>Järeldused</p> <ul style="list-style-type: none"> <li>• Makroskoopiliselt ei tuvastatud 12, 15 ja 18 kuud pärast implanteerimist nekrootilisi, degeneratiivseid ega trombootilisi nähte.</li> <li>• Sisemise ja välimise ketta lagunemine näis 12–18 kuu vahel olevat pooleli ja 18 kuu järel lõppenud, implanteeritud ala kattis valkjas kude.</li> <li>• Histoloogiliselt ei olnud pärast 18 kuu möödumist polümeermaterjal enam nähtav, kuid eksisteeris valendikuisene fibrooskude. Nekrootilisi, degeneratiivseid ega trombootilisi kahjustusi ei tuvastatud.</li> </ul> |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002 Radi Medical System AB</p> <p>Teostanud Biomatech, Prantsusmaa</p> | <p>Loomkatse; uurimuslik uuring</p> | <p>Uuringu eesmärk oli hinnata veresoonkonnas hemostaasi saavutamiseks ette nähtud biolaguneva implantaadi biosobivust.</p> | <p>Järelkontroll (pärast implanteerimist)</p> <ul style="list-style-type: none"> <li>• 12 nädalat</li> <li>• 24 nädalat</li> <li>• 36 nädalat</li> </ul> <p>N = 12 lammast, 3 looma ajapunkti kohta, 3 varulooma eutaneeritud 12, 15 ja 18 kuu möödudes</p> <p>Implanteerimiskohad – parem ja vasak reiearter, parem ja vasak ühisunearter</p> <p>Värvidoppler-ultraheliuuring</p> | <p><u>Une- ja reiearterite avatus 4 nädala möödudes</u></p> <ul style="list-style-type: none"> <li>• Suur verevoolu vähenemine 0/12 (0%)</li> </ul> <p><u>Suur verevoolu vähenemine puudub</u></p> <ul style="list-style-type: none"> <li>• Seadme sisestamisega seotud verevoolu raske häirimine 0/12 (0%)</li> <li>• Verevoolu vähenemine vasakus ühisunearteris 2/12 (16,6%) ajutise arteriaalse vasospasmi tõttu (seostatakse operatsiooni, mitte seadmega)</li> </ul> <p><u>Verevoolu halvenemine järelkontrolli andmetel</u></p> <p>12 nädalat – 0/12 (0%)</p> <p>24 nädalat – 0/12 (0%)</p> <p>36 nädalat – 0/12 (0%)</p>                                                 |

|  |  |  |  |  | <p>Vererõhu mõõtmine (3 lammast – 36 nädalat)</p> <ul style="list-style-type: none"> <li>Suurt verevoolu vähenemist ei tuvastatud</li> </ul> <p>Makroskoopilised andmed integratsiooni ja lagunemise kohta (aste 0–4)</p> <p><u>Unearteri paikmed</u></p> <p><i>Sisekül</i></p> <p>- kapseldumine</p> <p>12. nädal 1,3</p> <p>24. nädal 0,8</p> <p>36. nädal 0,7</p> <p>- materjali lagunemine</p> <p>12. nädal 2,2</p> <p>24. nädal 2,3</p> <p>36. nädal 0,7</p> <p><i>Väliskül</i></p> <p>- kapseldumine</p> <p>12. nädal 2,0</p> <p>24. nädal 1,0</p> <p>36. nädal 0,8</p> <p>- materjali lagunemine</p> <p>12. nädal 2,0</p> <p>24. nädal 2,7</p> <p>36. nädal 3,2</p> <p><u>Reiearteri paikmed</u></p> <p><i>Väliskül</i></p> <p>- kapseldumine</p> <p>12. nädal 1,0</p> <p>24. nädal 2,7</p> <p>36. nädal 1,0</p> <p>- materjali lagunemine</p> <p>12. nädal 2,0</p> <p>24. nädal 2,4</p> <p>36. nädal 3,0</p> <p><i>Sisekül</i></p> <p>- kapseldumine</p> <p>12. nädal 2,0</p> <p>24. nädal 1,2</p> <p>36. nädal 1,0</p> <p>- materjali lagunemine</p> <p>12. nädal 1,0</p> <p>24. nädal 2,2</p> <p>36. nädal 3,0</p> |
|--|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | <p><u>Histoloogilised andmed</u><br/> <u>integreerumise, lagunemise ja</u><br/> <u>põletikuparameetrite kohta</u><br/> <u>(asjakohaste väärtuste</u><br/> <u>keskmine, indeks 0–4) n = 6</u></p> <p><u>Unearteri paikmed</u><br/> Väline fibroos<br/> 12. nädal – 2,3<br/> 24. nädal – 2,3<br/> 36. nädal – 1,8<br/> Sisemine neointima<br/> 12. nädal – 3,0<br/> 24. nädal – 2,7<br/> 36. nädal – 3,3<br/> Materjali lagunemine<br/> 12. nädal – 1,7<br/> 24. nädal – 3,0<br/> 36. nädal – 3+<br/> Põletikuparameetrid<br/> (makrofaagid)<br/> 12. nädal – 3,0<br/> 24. nädal – 1,7<br/> 36. nädal – 1,7<br/> <u>Reiearteri paikmed</u><br/> Väline fibroos<br/> 12. nädal – 1,3<br/> 24. nädal – 1,5<br/> 36. nädal – 1,7<br/> Sisemine neointima<br/> 12. nädal – 3,7<br/> 24. nädal – 3,3<br/> 36. nädal – 3,8<br/> Materjali lagunemine<br/> 12. nädal – 2,0<br/> 24. nädal – 3,0<br/> 36. nädal – 3+<br/> Põletikuparameetrid<br/> (makrofaagid)<br/> 12. nädal – 3,5<br/> 24. nädal – 1,8<br/> 36. nädal – 1,8<br/> <u>Histomorfoloogilised avatuse</u><br/> <u>väärtused</u><br/> Unearteri paikmed<br/> 12. nädal – 74,0%<br/> 24. nädal – 81,9%<br/> 36. nädal – 89,43%<br/> Reiearteri paikmed</p> |
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|                                                                                                                                                                                                                                                                 |                                                                            |           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|-----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                                                                                 |                                                                            |           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                 | 12. nädal – 42,2%<br>24. nädal – 73,21%<br>36. nädal – 78,71%<br><br><u>Soone avatus ultraheliuuringul (keskmise %)</u><br>Unearteri paikmed<br>12. nädal – 94,6%<br>24. nädal – 96,7%<br>36. nädal – 94,7%<br>Reiearteri paikmed<br>12. nädal – 66,9%<br>24. nädal – 63,6%<br>36. nädal – 75,1%<br><br>Järeldused <ul style="list-style-type: none"> <li>12., 24. ega 36. nädalal olulisi lokaalse talumatuse märke ei tuvastatud (puudusid nähtavad põletikulised, nekrootilised või degeneratiivsed kahjustused).</li> <li>Puudusid peremeesorganismi või seadmega seotud olulised ebasoodsad koereaktsioonid</li> <li>36 nädala möödudes oli implantaadi lagunemine peaaegu lõppenud</li> </ul> |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France). | 2002<br><br>Radi Medical System AB<br><br>Teostanud Biomatech, Prantsusmaa | Loomkatse | Uuringu eesmärk oli hinnata bioühilduvust ja biofunktsionaalsust biolagunevas implantaadis, mis on ette nähtud hemostaasi tekitamiseks veresoonekonnas. Testitud seade oli ette nähtud sisestamiseks arteriseina punktsiooniavasse ja hemostaasi tekitamiseks. Üks ketas sisenes arteri punktsiooniavasse ja teine tõmbas sisemise ketta arteri välisküljelt pingule. Mõlemad kettad sisestati sisestuskanüüli kaudu. Plaadid olid ette nähtud ära hoidma veritsust, sulandudes paranemise käigus veresoone seina, | Implanteerimisperiood/järelkontroll on kõigi loomade puhul 5 nädalat<br><br>4 lammast, 1 siga<br><br>14 sulgemiselementi<br><br>8 sulgemiselementi implanteeriti 2 lambale,<br><br>2 sulgemiselementi implanteeriti 1 seale<br><br>Kui samasse reiearterisse implanteeriti kaks | Registreeriti kõik kõrvaltoimete kriteeriumid (põletik, nekroos, verejooks või muud kahjustused) ja õhukese pseudointima kihi teke. Erilist tähelepanu pöörati seadme esmasele koeintegratsioonile, eelkõige sisemise ketta kapseldumisele.<br><br>Makroskoopiliselt ei täheldatud olulist kohalikku talumatust ega trombi teket. Pärast sulgemiselementide implanteerimist reiearteritesse ei ilmnunud makroskoopilisel vaatlusel                                                                                                                                                                                                                                                                  |

|  |  |  | ning lõpuks lagunema ja resorbeeruma. Uuringu eesmärk oli koguda ja analüüsida andmeid pärast seadme funktsionaalset implanteerimist lambale ja seale, et hinnata implantaadi võimekust säilitada füsioloogilist funktsiooni kasutamisel vereringesüsteemis, määrata peremeeslooma reaktsioon ja seadme reaktsioon (füüsiline terviklikkus, koesse kapseldumine eutaneerimis) ning hinnata implantaadi lagunemist. | sulgemiselementi, implanteeriti need > 30 mm vahega | <p>mingit erinevust lammaste ja sea vahel. Makroskoopiliselt ei täheldatud olulist kohalikku talumatust ega trombi teket. Pärast sulgemiselementide implanteerimist reicararteritesse ei ilmnunud makroskoopilisel vaatlusel mingit erinevust lammaste ja sea vahel.</p> <p>Lammaste implantatsioonikoha histopatoloogiline analüüs ei näidanud lokaalseid kõrvaltoimeid. Sise- ja välisketastel ilmnis lagunemise märke ning osal juhtudel olid need purunenud väiksemateks osadeks. Sisemised kettad olid täielikult integreerunud neointima koesse. Seal näitas histopatoloogiline analüüs sise- ja välisketaste ümbruses veidi rohkem põletikutunnuseid. Mõlemal loomal näitas multifilament veidi rohkem põletikutunnuseid kui ketta materjal, mis on põimitud õmblusmaterjali puhul suurema pindala tõttu normaalne.</p> <p>Soone avatust mõõdeti 5 nädala pärast, kasutades kolme eri meetodit: histomorfomeetriline, histomorfomeetriline koos soone läbimõõdu mõõtmisega nihiku abil ning värvidoppler-ultraheliuuringuga. Keskmise soone avatus lambal oli vahemikus 60–80%, olenevalt meetodist</p> |
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|                                                                                                                                                                                                              |                              |                                             |                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                | (12 vaatlust). Seal oli keskmine veresoone avatus 40–80% (2 vaatlust).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|---------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Esimene kliiniline uuring inimesel</b>                                                                                                                                                                    |                              |                                             |                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Uuringu nimetus                                                                                                                                                                                              | Aasta/asutus                 | Uuringu tüüp                                | Eesmärgid                                                                                                                                                                                                                                                                                                            | Põhitulemused                                                                                                                                                                                                                                                                                                                                  | Võimalikud aktsepteerimiskriteeriumid                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Avatud ühe rühmaga mitmekeskuse line uuring | Uuringu eesmärk oli määrata FemoSeal Vascular Closure Systemi (FemoSeal Systemi) ohutus, jõudlus ja efektiivsus üldiselt ning spetsiifiliselt sulgemiselementidega seoses patsientidel, kellele tehti südamediaagnostika või interventsionaalseid kardioloogilisi protseduure, kasutades ligipääsu reiearteri kaudu. | 2-osaline uuring<br>Kokku n = 80<br>1. osa n = 20<br>2. osa n = 60<br>Näidustused<br>1. osa – diagnostiline südame kateteriseerimine, kasutades ligipääsu reiearteri kaudu<br>2. osa – diagnostiline südame kateteriseerimine ja interventsionaalkardioloogilised protseduurid, kasutades ligipääsu reiearteri kaudu<br>30 päeva järelkontroll | Tulemused<br><u>- hemostaas saavutatud FS-iga ilma kompressioonita</u><br>- 1. osa 20/20 (100%)<br>- 2. osa 58/60 (97%)<br>Hemostaasini kulunud mediaanaeg protseduuri vältel (2. osa) – 1,0 minutit (vahemik: kohe kuni 8 minutit)<br><u>Aeg liikuma hakkamiseni (minutites)</u><br>1. osa – mediaan: 33,0<br>keskmine: 67,8<br>2. osa – mediaan: 45<br>keskmine: 87,5<br><u>Raskete vaskulaarsete tüsistuste avaldumus – 30 päeva järelkontroll</u><br>1. osa<br>- veresoonekonna tüsistusteta 20/20 (100%)<br>2. osa<br>- pseudoaneurüsm 1/59 (1,69%)<br><u>Ravi ebaõnnestumine</u><br>1. osa – 0/20 (0%)<br>2. osa – 3/60 (5%)<br>• 2 juhul ei saavutatud hemostaasi ilma kompressioonita |

|  |  |  |  |  | <ul style="list-style-type: none"> <li>1 juhul raske vaskulaarne tüsistus, pseudoaneurüsm</li> </ul> <p><u>Püsiv immitsemine</u></p> <p>1. osa – 0/20 (0%)</p> <p>2. osa – 8/60 (13%)</p> <p><u>Hematoom</u></p> <p>1. osa – 0/20 (0%)</p> <p>2. osa – 6/60 (10%)</p> |
|--|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Osana FemoSeal™ VCS-i turuletoomiseelsest arenduskavast viidi läbi 3 funktsionaalset loomkatset. 2000. aastal enne kliiniliste uuringute alustamist viidi läbi loomkatse, et hinnata FemoSeal™ VCS-i biofunktsionaalsust. Selles uuringus hinnati sulgemiselementide võimet säilitada füsioloogilist funktsiooni ja hinnati nende lagunemist. 18 kuu möödudes ei olnud sisemise ja välimise ketta materjal enam nähtav ning oli asendunud valendikusisese fibrooskoega. Kokkuvõttes sai kinnitust FemoSeal™ VCS-i sulgemiselemendi võime säilitada füsioloogilist funktsiooni kasutamisel vereringesüsteemis.

2002. aasta loomkatse eesmärk oli hinnata bioühilduvust ja biofunktsionaalsust biolagunevas implantaadis FemoSeal™ VCS, mis on ette nähtud hemostaasi saavutamiseks veresoonekonnas. Kokkuvõttes lagunes implantaat peaaegu täielikult 36 nädalaga ja ühtegi olulist ebasoodsat koereaktsiooni ei esinenud.

Teise 2002. aasta loomkatse eesmärk oli hinnata bioühilduvust ja biofunktsionaalsust biolagunevas implantaadis FemoSeal™ VCS, mis on ette nähtud hemostaasi saavutamiseks veresoonekonnas. 5 nädalaga oli ketas täielikult kapseldunud ning nii sisemise kui ka välimise ketta puhul täheldati lagunemise märke. Kokkuvõttes sai kinnitust implantaadi võime säilitada füsioloogilist funktsiooni kasutamisel vereringesüsteemis.

Osana FemoSeal™ VCS-i kliinilisest arenduskavast viis Radi Medical System AB läbi turustamiseelse kliinilise uuringu. Seda kliinilist uuringut ei ole avaldatud ja see ei ole veebis saadaval. Uuring seadme mudeliga nr 11200 viidi läbi aastatel 2002–2004 Euroopa standardi EN 540 (meditsiiniseadmete kliiniline uuring inimestel) alusel ja kooskõlas ICH kliiniliste uuringute ja heade kliiniliste tavade üldiste kaalutlustega. Uuringu üksikasjad on dokumenteeritud aruandes EU-SE-001. See kliiniline uuring dokumenteeriti Radi Medical Systems AB lõpparuandes „Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures” (mitmekeskuseline kliiniline uuring reiarteri punktsiooni sulgemiseks pärast

diagnostilisi/interventsionaalseid reiearteri punktsioone FemoSeal Vascular Closure Systemiga). See kliiniline uuring viidi läbi FemoSeal™-i esimese mudeliga nr 11200 ja keskendus implanteeritavate sulgemiskomponentide ohutusele ning efektiivsusele. Ainus erinevus esimese mudeli nr 11200 ja praeguse mudeli C11202 vahel on Fr-suurus, vastavalt 6 Fr ja 7 Fr, ja täiustatud paigaldussüsteem. Kliinilised eelised, ettenähtud kasutus, tööpõhimõtted ja implanteeritavate sulgemiselementide, sisemise sulguri ja välimise lukustusplaadi toormaterjalid on samad.

Seade on ette nähtud kasutamiseks patsientidel, kellele on tehtud südame diagnostiline või interventsionaalne protseduur, kasutades ligipääsuks reiearterit. Selle uuringu eesmärk oli teha kindlaks FemoSeal™ VCS-i ohutus, toimivus ja efektiivsus. See oli prospektiivne, mitmekeskuseline, ühe rühmaga avatud uuring 30-päevase järelkontrolliga.

Esmane tulemusnäitaja oli aeg kuni hemostaasini, mis määratleti tugeva verejooksu puudumisena. Esmane ohutuse tulemusnäitaja oli raskete vaskulaarsete tüsistuste avaldumus 30 päeva jooksul. Teisesteks tulemusnäitajateks olid aeg kuni liikuma hakkamiseni, ravi ebaõnnestumiste osakaal, kõrvalnähtude avaldumus ja seadme toimivuse näitajad sisseviimise ja vabastamise ajal.

Sellesse uuringusse kaasatud patsiendid olid täiskasvanud, kes suutsid anda teadva nõusoleku ja kellel oli vähemalt üks intaktne jalgaseljaarteri pulss. Patsiendid jäeti uuringust välja, kui neil oli mõni järgmistest seisunditest.

- Anamneesis perifeerne vaskulaarne haigus
- Autoimmuunhaigus
- Teadaolev raske aneemiline veritsushäire
- INR > 1,5
- Müokardiinfarkt 72 tunni vältel
- Ravile allumatu hüpertensioon
- Rasvumus, mis välistab ligipääsu Seldingeri tehnika abil
- Veresoonesiirik või stent arteriotoomia kohas
- Varasem ipsilateraalne punktsioon 3 kuu jooksul
- Eeldatav elumus < 6 kuud

Lisaks uuriti patsiente operatsiooni ajal ja nad jäeti uuringust välja, kui täheldati mõnda järgmistest olukordadest.

- Ühisreiearteri valendiku läbimõõt < 5 mm
- Arteriharud 2 cm punktsioonikohast proksimaalsel

- Oluline stenoos kuni 3 cm kaugusel punktsioonikohast
- > 6 Fr primaarse sisestuskanüüli kasutamine
- Punktsioon reiearteri bifurkatsioonil või sellest distaalsel
- Mitu reiearteri punktsiooni
- Teadaolev või kahtlustatav reiearteri tagaseina punktsioon
- Suur hematoom (2:6 cm) protseduuri lõpetamisel
- Keeruline esmase protseduurikanüüli sisestamine, mis on tingitud väänilisest koest või veresoonest

See ühe uuringuplaaniga uuring viidi läbi kahes osas. 1. osas registreeriti 20 patsienti, seejärel tehti ohutusanalüüs ja 2. osas registreeriti veel 60 patsienti.

1. osas registreeritud patsientide keskmine vanus oli 65,9 aastat, 70,0% patsientidest olid mehed ja 95% patsientidest said samaaegselt ravimeid. 2. osas registreeritud patsientide keskmine vanus oli 63,8 aastat, 78% patsientidest olid mehed ja 100% patsientidest said samaaegselt ravimeid.

Uuringusse kaasamiseks sobisid patsiendid, kellele tehti diagnostilisi (1. ja 2. osa) või interventsionaalseid (2. osa) südame kateteriseerimisprotseduure. Protseduurid olid kooskõlas kõigi patsiente uuringusse registreerivate haiglate ravistandardiga ning seejärel kasutati FemoSeal™ VCS-i. Patsiendiandmeid koguti ravieelselt, protseduuri ajal ning 1. ja 30. päeval pärast protseduuri. Tulemused on kokku võetud **tabelis 1.5** ja näitavad, et FemoSeal™ VCS on selles patsiendirühmas kasutamiseks ohutu ja efektiivne.

**Tabel 1.5. Turustamiseelse uuringu kliinilised tulemused**

|                                                                                                                          | 1. osa       | 2. osa                    |
|--------------------------------------------------------------------------------------------------------------------------|--------------|---------------------------|
| Patsientide arv                                                                                                          | 20           | 60                        |
| Keskmine aeg hemostaasini                                                                                                | 1,2 minutit  | 1,6 minutit <sup>a</sup>  |
| Keskmine aeg kõndima hakkamiseni                                                                                         | 72,2 minutit | 87,5 minutit <sup>b</sup> |
| Suurte vaskulaarsete tüsistuste avaldumus <sup>c</sup>                                                                   | 0 (0%)       | 1 (2%)                    |
| Kõrvalnähtudega patsientide arv                                                                                          | 5 (25%)      | 19 (32%)                  |
| Ravi ebaõnnestumine (määratletud kui suured vaskulaarsed tüsistused, vajadus manuaalse kompressiooni järele või mõlemad) | 0 (0%)       | 3 (5%)                    |
| Seadme tõrge                                                                                                             | 0 (0%)       | 6 (10%)                   |

*<sup>a</sup>Lähtuvalt 58-patsiendilisest valimist, sest 2 patsienti ei saavutanud varasemate ipsilateraalsete punktsioonide tõttu protseduuri ajal hemostaasi. Nende patsientide puhul saavutati hemostaas 7 ja 37 minuti pärast.*

*<sup>b</sup>Lähtuvalt 59-patsiendilisest valimist: 1 patsienti ei võetud arvesse, sest ta pandi kopsuturse tõttu hingamisaparaadi alla ega suutnud enam kui nädala jooksul kõndima hakata.*

*<sup>c</sup>Määratletud kui vaskulaarne tüsistus, mis vajab vereülekannet või kirurgilist ravi, või lokaalne infektsioon, mis vajab antibiootikumi, haiglaravi või haiglaravi pikendamist või haava kirurgilist puhastamist.*

Uuringu 1. osas ei täheldatud suuri vaskulaarseid tüsistusi. Uuringu 2. osas teatati 1 suurest vaskulaarsest tüsistusest: pseudoaneurüsm, millest teatati 1 päeva jooksul pärast protseduuri. Vajalikuks osutus ultraheliga juhitud kompressioon ja trombiini süstimine pseudoaneurüsmi, samuti patsiendi haiglaravi pikendamine.

Viie uuringu 1. osas teatatud kõrvalnähust 1 oli potentsiaalselt seadmega seotud: mittetõsine tugeva verejooksu juhtum 1 päev pärast protseduuri. Uuringu 2. osas esinenud 19 kõrvalnähust olid 3 seadmega seotud mittetõsised hematoomid ning lisaks täheldati 6 potentsiaalselt seadmega seotud mittetõsist kõrvalnähtu, sh 3 püsivat veritsust, 2 hematoomi ja 1 säärevalu pärast kehalist aktiivsust.

2. osas peeti ravi ebaõnnestuks 3 patsiendil: 2 hemostaasi mittesaavutamise tõttu ilma kompressioonita ja 1 suure vaskulaarse tüsistuse (pseudoaneurüsmi) tõttu. Uuringu 1. osas ravi ebaõnnestumisi ei esinenud.

Uuringu 2. osas esines kuus seadme tõrget, kolm ei häirinud protseduuri, üks oli tingitud kasutaja veast, üks oli sisestuskanüüli leke ja ühe puhul murdus filamendi kinnitus. Kaks viimast probleemi kõrvaldati C11202 mudeli uuendustega.

Turuletoomiseelse kliinilise uuringu 2. osas ei teatatud patsientide ravijärgimatuse tõttu 6 kuu järelkontrolli tulemusi. Turustamiseelse kliinilise uuringu (EU-SE-001) 30 päeva tulemused, mis on kooskõlas kliinilises kirjanduses nimetatud järelkontrolli ajaga, näitavad, et FemoSeal™ VCS on ohutu ja efektiivne.

#### **1.4.2 Turustamisjärgsete kliiniliste uuringute andmete kokkuvõte**

Allolevas **tabelis 1.6** on kirjeldatud 4 lõpetatud turustamisjärgset kliinilist uuringut. Neid kliinilisi uuringuid ei ole avaldatud ja need ei ole saadaval internetis.

Tabel 1.6 Lõpetatud turustamisjärgsed kliinilised uuringud

| Lõpetatud turustamisjärgsed kliinilised uuringud                                            |                                                        |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|---------------------------------------------------------------------------------------------|--------------------------------------------------------|-----------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|----|-----|----------|-------|----------|-----------|----|----------|-----------|-------------------------|----------|--------------------|------------|---------------------|-----------|-------------------|---------|-----------------------|----------|--------------------------------|----------|----------------------|-----------|--------------------------|-----------|-----------------------------------|----------|----------------------|--------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Uuringu nimetus                                                                             | Aasta/asutus                                           | Uuringu tüüp                                                    | Eesmärgid                                                                                                                                                                                                                                                                                                                                                                                                          | Põhitulemused                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Võimalikud aktsepteerimiskriteeriumid                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br><br>RADI                                       | Turustamisjärgne uuring, uue pakendi vastuvõetavus kasutajatele | Turustamisjärgne uuring funktsionaalsuse dokumenteerimiseks viidi läbi FemoSeal® Vascular Closure Systemi mudeliga number 11202, mille paigaldussüsteemi on esimese mudeliga nr 11200 võrreldes muudetud.<br><br>Uuringu eesmärk oli saada tagasisidet muudetud kasutusjuhendile, arstide ja õdede koolitusprojektile, kinnitada riskianalüüsiga saadud hinnangut ning anda sisendit toote kvaliteediparandusteks. | 100 patsienti <ul style="list-style-type: none"><li>63 meest / 37 naist</li><li>Keskmine vanus naistel 68 aastat, meestel 65 aastat</li></ul><br>2 Rootsi haiglat, 6 arsti<br><br>112 seadet<br><br>Patsiendikirje vormidesse (CRF) salvestatud andmed<br><br>Kavandatud jälgimisaeg – 30 minutit pärast paigaldamist                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Tulemused<br><br>1. Kasutusjuhendis esitatud joonised/juhised on informatiivsed ja piisavad<br><br>2. Kohene hemostaas (91/100) |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)           | Dr Nicolas Moes, Innsbrucki Meditsiiniülikool, Austria | Turustamisjärgne kinnitav hindamine                             | Selle uuringu eesmärk oli hinnata FemoSeal®-i ohutust ja toimivust kliinilises tavaolukorras kasutatuna patsientidel, kellele tehti diagnostiline südame kateteriseerimine või perkutaanne kardioloogiline interventsiooniprotseduur 7 Fr kanüüliga.                                                                                                                                                               | 50 järjestikust patsienti<br><br>Näidustus – diagnostiline või invasiivne südame kateteriseerimine ühisreiarteri kaudu<br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yr)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                               | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yr) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Esmased tulemusnäitajad <ul style="list-style-type: none"><li>Esmase efektiivsuse tulemusnäitaja – TTH (aeg hemostaasini), koos vere immitsemisega või ilma, kuid manuaalse või mehaanilise lisakompressioonita.</li><li>Ohutuse tulemusnäitaja – kõrvalnähtude avaldumus – väikesed ja suured vaskulaarsed tüsistused ja kõik muud kõrvalnähud – tõsised ja mittetõsised uuringu kestel (st kuni patsiendi väljakirjutamiseni).</li></ul><br>Tulemused <ul style="list-style-type: none"><li>Keskmine aeg hemostaasini</li><li>Diagnostika 56,6 ± 29 sekundit</li><li>Interventsioon 59,9 ± 16,2 sekundit</li><li>Kõik patsiendid 57,8 ± 26,3</li><li>Kõik patsiendid võisid pärast 4-tunnist lamamist probleemideta kõndima hakata.</li></ul> |
| n                                                                                           | 50                                                     |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| men                                                                                         | 35 (70%)                                               |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| women                                                                                       | 15 (30%)                                               |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| PCI cases                                                                                   | 15                                                     |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| age (yr)                                                                                    | 62.8±11.1                                              |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| body mass index (kg/m²)                                                                     | 25.4±6.7                                               |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| systolic BP (mmHg)                                                                          | 131.2±20.9                                             |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| diastolic BP (mmHg)                                                                         | 77.9±10.6                                              |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| diabetes mellitus                                                                           | 9 (18%)                                                |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| arterial hypertension                                                                       | 34 (68%)                                               |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| previous coronary intervention                                                              | 13 (26%)                                               |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| preprocedure aspirin                                                                        | 50 (100%)                                              |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| preprocedure clopidogrel                                                                    | 50 (100%)                                              |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Procedural unfractionated heparin                                                           | 15 (30%)                                               |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Procedural abciximab                                                                        | 2 (4%)                                                 |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                 |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |



|                                                                                                                                 |                                 |                                                               |                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
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|                                                                                                                                 |                                 |                                                               |                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <p>Ohutuse tulemused</p> <ul style="list-style-type: none"> <li>49/50 (98%) ilma vaskulaarsete tüsistusteta kuni haiglast väljakirjutamiseni</li> <li>Keskmine aeg väljakirjutamiseni 2,6 päeva</li> <li>1/50 (2%) väike verejooks järgmisel päeval pärast probleemideta liikumist angiograafia päeval</li> </ul>                                                                                                                                                                                                                                                                     |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | 2009 RADI                       | Turustamisjärgne uuring                                       | <p>Uuring peaks näitama, kas klientidel/kasutajatel esines probleeme uue pakendiga, eeskätt Tuvek/PET-PE-koti mittesteriilse välisküljega.</p> <p>Samuti peaks uuring näitama, kas raviarst tajub seadme kasutus-/paigaldusetappides erinevusi võrreldes varem kasutatud seadmetega.</p> <p>Uuring peaks andma teavet toote kvaliteedi edasise parandamise vajaduse kohta.</p> | <p>25 seadet</p> <p>4 Rootsi haiglat</p> <p>16/25 (64%) patsientidest olid läbinud PKI ja said tugevat antikoagulantravi</p>                                                                                                                                                                                                                                                                                                                                                 | <p>Tulemused</p> <ol style="list-style-type: none"> <li>Pakendiga seotud probleemid – 21/25 (84%) kasutuskorda olid edukad; 4/25 (16%) ebaõnnestus (1 uue sisestaja katsetamine, 1 juhul tuli siseketta nupp pärast arteriotoomia läbimist tagasitõmbeetapis üles ning välisketas asetus sisselõike koekanalisse; 2 juhul ei saavutatud kohest hemostaasi, ehkki paigaldusprobleeme ei tekkinud).</li> <li>Kohene hemostaas 19/25 (76%) patsiendil</li> <li>Veritsus 11/25 (44%) – 9/25 (36%) immitsemine/veritsus, 2/25 (8%) hematoomid</li> </ol> <p>Kõrvalnähtude kogumäär 19%</p> |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022) | 2022/Terumo Medical Corporation | Prospektiivne mitmekeskuseline turustamisjärgne vaatlusuuring | <p>Senisest paremini näidata FemoSeal™ VCS-i ohutust ja efektiivsust ühisreiarteri ligipääsukoha hemostaasi saavutamisel kliinilistes tavatingimustes patsientidel, kellele tehakse perkutaanseid endovaskulaarseid protseduure.</p>                                                                                                                                           | <ul style="list-style-type: none"> <li>Patsiendi järelkontroll 30 päeva möödudes (<math>\pm 7</math> päeva) haiglavisiidi või telefonikõne teel.</li> <li>Registreerimine: detsember 2021 kuni juuli 2022.</li> <li>230 osalejat, kellele tehakse diagnostiline või interventsionaalne endovaskulaarne protseduur, milles kasutatakse FemoSeal™-i.</li> </ul> <p>3 uuringukeskust Euroopas: Prantsusmaa (92 patsienti), Saksamaa (38 patsienti), Belgia (100 patsienti).</p> | <ul style="list-style-type: none"> <li><b>Demograafilised andmed / kaasuvad haigused</b></li> <li>- Sugu: 161 meest (70%) / 69 naist (30%).</li> <li>- Keskmine vanus: <math>70 \pm 12</math>.</li> <li>- KMI: <math>26,1 \pm 4,95 \text{ kg/m}^2</math>.</li> <li>- Hüpertensioon: 160 patsienti (69,6%).</li> <li>- Düslipideemia: 128 (55,7%).</li> <li>- Pärgarteri haigus: 42 (18,3%).</li> <li>- Praegune suitsetaja: 86 (37,6%).</li> <li>- Varasem suitsetaja: 66 (28,8%).</li> <li>- Südame isheemiatõbi: 34 (14%).</li> </ul>                                               |

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|  |  |  |  |  | <ul style="list-style-type: none"> <li>- Varasem müokardiinfarkt: 18 (7,8%).</li> <li>- Perifeerse arteri revaskularisatsioon: 12 (5,2%) unearter ja 83 (37,5%) ja alajäseme arter.</li> <li>- Antiagregantravi (uuringu alguses): 211 (91,7%), sh 21 (9,1%) kaksikantiagregantravi (DAPT).</li> <li>- Suukaudne antikoagulatsioon: 40 (17,4%) patsienti.</li> <li>• <b>Interventsiooni karakteristikud</b> <ul style="list-style-type: none"> <li>- Keskkond: statsionaaris 162 juhtu (70,4%), ambulatoorses kliinikus 68 juhtu (29,6%).</li> <li>- Valdav näidustus: klaudikatsioon 147 juhtu (63,9%).</li> <li>- Meetod: 35 antegraadset (15,3%), 194 retrograadset (84,7%).</li> </ul> </li> <li>• <b>Esmased tulemusnäitajad</b> <ul style="list-style-type: none"> <li>- Kombineeritud ohutuse (juurdepääsukoha jäseme suurte tüsistuste puudumine 6 tunni jooksul pärast protseduuri) ja efektiivsuse (edukas punktsioonikoha hemostaas) tulemusnäitaja saavutati 215/226 patsiendil (95,1%) [95% CI: 91,46; 97,55] täielikus analüüsirühmas ja 215/230 patsiendil (93,5%) [95% CI: 89,47; 96,30] FemoSeal™-iga ravitud rühmas.</li> <li>- Efektiivsuse tulemusnäitaja saavutati</li> </ul> </li> </ul> |
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|  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|--|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <p>219/226 (96,9%) CI [93,7; 98,7] patsiendil.</p> <p>- Ohutuse tulemusnäitaja saavutati 220/230 patsiendil (95,2%) [95% CI: 92,15; 97,90].</p> <p>• <b>Teisesed tulemusnäitajad</b></p> <p>- Väiksemate juurdepääsukoha tüsistuste puudumine 6 tunni jooksul pärast protseduuri saavutati 225/230 patsiendil (97,8%) [95% CI: 95,00; 99,29].</p> <p>- Suuremate ja väiksemate juurdepääsukoha tüsistuste puudumine 6 tunni kuni 30 päeva jooksul pärast protseduuri saavutati 219/230 patsiendil (95,2%) [95% CI: 91,60; 97,59]</p> <p>- Mediaanaeg hemostaasini FemoSeal™ VCD-ga: 0,42 (0,25; 0,50) minutit.</p> <p>- Mediaanaeg kõndima hakkamiseni: 5,00 (4,54; 5,50) minutit.</p> <p>- Haiglaravi kestuse mediaan: 23,98 (22,72; 25,00) tundi.</p> <p>- FemoSeal™ VCS-i kasutatavus: „lihtne“ või „väga lihtne“ paigaldada 98,7% juhtudest („lihtne“ paigaldada 21 (9,2%), „väga lihtne“ paigaldada 205 (89,5%) juhul), 226 (98,3%) juhul takistus paigaldamisel vähene või puudub.</p> <p>152/230 (66,1%) patsiendist, keda raviti FemoSeal™-i komplekti kuuluva ja FemoSeal™-is soovitatud juhtetraadiga (GW 0,038"), ei teatanud seadme puudustest ega kõrvalnähtudest.</p> |
|--|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

2006. aasta uuring viidi läbi selleks, et kinnitada praeguse täiustatud paigaldussüsteemiga seadme ohutust ja efektiivsust ning saada tagasisidet FemoSeal™ VCS-i kasutusjuhendi ja koolitusprogrammi kohta. Uuring hõlmas 100 patsienti ja esmaseks tulemusnäitajaks oli see, kas hemostaas saavutati või läks vaja manuaalset või mehaanilist lisakompressiooni. Selles uuringus leiti, et FemoSeal™ VCS-i paigaldamine oli enamikel juhtudel edukas (91% saavutati kohene hemostaas).

2008. aasta uuringusse kaasati 50 patsienti, et hinnata FemoSeal™ VCS-i ohutust ja efektiivsust kasutamisel tavapärase kliinilise praktika käigus patsientidel, kellele tehti südame kateteriseerimine 7 Fr kanüüliga. Uuringu esmane tulemusnäitaja oli hemostaasiaeg ja liikumahakkamiseni kulunud aeg ilma manuaalse või mehaanilise lisakompressioonita. Uuringutulemused näitasid, et keskmine aeg hemostaasini oli 57,8 sekundit ning kõik patsiendid hakkasid liikuma pärast 4-tunnist voodipuhkust.

2009. aasta uuringu eesmärk oli hinnata uut FemoSeal™ VCS-i pakendit. Uuringusse kaasati 25 patsienti. Esmane tulemusnäitaja oli see, kas kasutajal tekkis pakendiga probleeme. Kasutajatel ei tekkinud uue FemoSeal™ VCS-i pakendiga probleeme. Selles uuringus koguti ka hemostaasini kuluva aja andmeid.

2022. aasta uuringu eesmärk oli koguda proaktiivselt ohutuse ja efektiivsuse andmeid FemoSeal VCS-i kohta ühisreiarteri ligipääsukoha hemostaasi saavutamisel kliinilistes tavatingimustes patsientidel, kellele tehakse perkutaanseid endovaskulaarseid protseduure. Uuringusse kaasati 230 patsienti. Registriuuringu esmased tulemusnäitajad on protseduuri edukus (st edukas hemostaas punktsioonikohas) ja suuremate tüsistuste (nt veresoonevigastus, ligipääsukohaga seotud verejooks, ligipääsukoha infektsioon, korduv manuaalne kompressioon ja uue ligipääsukohaga seotud ipsilateraalne alajäseme äge isheemia) arvu vähenemine. Uuringus jõuti järeldusele, et FemoSeal™ VCS toimib hästi reaalsetes tingimustes ning tagab efektiivse hemostaasi ja juurdepääsukoha tüsistuste madala määra perifeerseid endovaskulaarseid sekkumisi läbivatel patsientidel. Sellel on hea toimivus koos lühikese hemostaasini kuluva ajaga ja hea kasutajasõbralikkuse tagasisidega, mis muudab FemoSeal™ VCS-i väärtuslikuks seadmeks femoraalse juurdepääsu sulgemisel.

### **1.4.3 Turustamisjärgsete kliiniliste jätku-uuringute andmete kokkuvõte**

#### **1.4.3.1 Lõpetatud turustamisjärgne kliiniline järelkontroll**

Kokkuvõte lõpetatud turustamisjärgse kliinilise järelkontrolli toimingutest on esitatud allolevas tabelis 1.7.

**Tabel 1.7. Turustamisjärgse kliinilise järelkontrolli toimingud**

| Lõpetatud turustamisjärgse kliinilise järelkontrolli toimingud            |              |                                                         |                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|---------------------------------------------------------------------------|--------------|---------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Toimingu nimetus                                                          | Aasta/asutus | Uuringu tüüp                                            | Eesmärgid                                                                                                                                                                                                                                                        | Põhitulemused                                                                                                                                                                                                                                                                                                                    | Võimalikud aktsepteerimiskriteeriumid                                                                                                                                                                                                                                                                                                                                                                                                                              |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021 TMC     | Turustamisjärgne kliiniline uuring - kvaliteetne uuring | Turustamisjärgne uuring, et mille eesmärk oli koguda prospektiivset tagasisidet seoses Euroopa Liidu turgudel levitatud FemoSeal™-i vaskulaarse sulgemisseadme kasutamisega.                                                                                     | <ul style="list-style-type: none"> <li>120 juhtumit</li> <li>8 arsti, kellel oli &gt; 5 aastat kogemusi</li> <li>Mitmed Euroopa riigid</li> </ul>                                                                                                                                                                                | <b>Seadme hindamine 1–5 skaalal – uuringu tulemused</b> <ul style="list-style-type: none"> <li>Sobivuskriteeriumid <ul style="list-style-type: none"> <li>Hindeid 3–5 loetakse soodsaks</li> <li>Kõikidel väidetel peab olema ≥ 80% positiivne tagasiside</li> </ul> </li> <li>Tulemused <ul style="list-style-type: none"> <li>Ükski küsitluse väide ei saanud &gt; 20% ebasoodsaid vastuseid</li> <li>Toote kohta ei ole esitatud kaebusi</li> </ul> </li> </ul> |
| 20210298 – 0,035" and 0038" Guidewire Clinical Survey Report (2021)       | 2021 TMC     | Turustamisjärgne kliiniline uuring - kvaliteetne uuring | Turustamisjärgne uuring, mille eesmärk oli koguda prospektiivset tagasisidet seoses 6 Fr Angio-Seal™ VIP Vascular Closure Device'iga (VCD) kaasasoleva 0,035-tollise juhtetraadi ja nii 8 Fr Angio-Seal™ VIP VCD kui ka FemoSeali vaskulaarse sulgemissüsteemiga | <ul style="list-style-type: none"> <li>Uuringud 0,035" traadi kohta <ul style="list-style-type: none"> <li>106 küsitlust</li> <li>64 arsti</li> </ul> </li> <li>Uuringud 0,038" traadi kohta <ul style="list-style-type: none"> <li>109 küsitlust</li> <li>55 arsti</li> </ul> </li> <li>12 retrospektiivset uuringut</li> </ul> | <b>Seadme hindamine 1–5 skaalal – uuringu tulemused</b> <ul style="list-style-type: none"> <li>Sobivuskriteeriumid <ul style="list-style-type: none"> <li>Hindeid 3–5 loetakse soodsaks</li> <li>Kõikidel väidetel peab olema ≥ 80% positiivne tagasiside</li> </ul> </li> <li>Tulemused <ul style="list-style-type: none"> <li>Kõik juhtetraadid said vastuvõetavad hinnangud</li> <li>Toote kohta ei ole esitatud kaebusi</li> </ul> </li> </ul>                 |

| Lõpetatud turustamisjärgse kliinilise järelkontrolli toimingud                                                                               |                  |                                                         |                                                                                                         |                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|----------------------------------------------------------------------------------------------------------------------------------------------|------------------|---------------------------------------------------------|---------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                              |                  |                                                         | kaasasoleva 0,038-tollise juhtetraadi kasutamisega Euroopa Liidu turgudel.                              |                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| FemoSeal <sup>TM</sup> Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024 TMC/TE | Turustamisjärgne kliiniline uuring - kvaliteetne uuring | Eesmärk oli koguda tagasisidet seoses FemoSeal VCS-i kasutamisega EL-i turul levitatud juhtetraatidega. | <ul style="list-style-type: none"> <li>• 126 küsitlust</li> <li>• 7 asukohta</li> <li>• 5 riiki</li> <li>• 14. november 2023-11. juuni 2024</li> <li>• Arsti eriala: <ul style="list-style-type: none"> <li>○ Veresoonekirurg</li> <li>○ Interventsionaalradioloog</li> <li>○ Angioloogia</li> </ul> </li> </ul> | <b>Seadme hindamine 5 palli skaalal – uuringu tulemused</b> <ul style="list-style-type: none"> <li>• Sobivuskriteeriumid <ul style="list-style-type: none"> <li>○ Hindeid 3–5 loetakse soodsaks</li> <li>○ Kõikidel väidetel peab olema <math>\geq 80\%</math> positiivne tagasiside</li> <li>○ Kui selles uuringus esineb kõrvaltoimeid, peavad need olema need, mida riskijuhtimine on eeldanud.</li> </ul> </li> <li>• Patsientide demograafilised andmed <ul style="list-style-type: none"> <li>○ Naised: 29,4% (37/126)</li> <li>○ Mehed: 69,8% (88/126)</li> <li>○ Sugu ei ole avaldatud: 0,8 (1/126)</li> <li>○ Vanus &gt; 75 aastat: 31,7%</li> </ul> </li> <li>• Tulemused <ul style="list-style-type: none"> <li>○ FemoSeal<sup>TM</sup> VCS-iga kaasas olev juhtetraat: 101/126 (80,2%).</li> </ul> </li> </ul> |

| Lõpetatud turustamisjärgse kliinilise järelkontrolli toimingud |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|----------------------------------------------------------------|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                |  |  |  |  | <ul style="list-style-type: none"> <li>○ Protseduuri kestus (minutites): 63,4 (36,6) (keskmine (SD)); 57,0 (36,0-81,0) (mediaan (IQR))</li> <li>○ Kõik FemoSeal™ VCS-i toimivuse hinnangud olid soodsad.</li> <li>○ Kõik FemoSeal™ VCS-iga kaasasolevate juhtetraatide hinnangud olid soodsad.</li> <li>○ Üks (0,8%) kõrvaltoime: FemoSeal™ VCS-i kettad ei olnud hästi joondatud tõenäoliselt jäiga juhtetraadi (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 tolli) kasutamise tõttu, mis vajab hemostaasi saavutamiseks manuaalset kompressiooni.</li> </ul> |

Terumo Medical Corporation on praeguse aruandlusperioodi jooksul (01. septembrist 2019 kuni 31. augustini 2024) läbi viinud kolm kvaliteetset arstide kasutajaküsitlust.

FemoSeal™-i kliiniliste küsimustikega koguti kliinilise kasutamise ajal proaktiivseid kliinilisi andmeid FemoSeal™ VCS-i ohutuse ja toimivuse kohta. Küsimustik sisaldas küsimusi, mis keskendusid seadmele üldiselt ja sellega seotud tarvikutele, sh 0,038-tolline juhtetraat, ja nende vahetule koostoimele. Juhtetraadi kliiniliste küsimustikega koguti proaktiivseid kliinilisi andmeid seoses FemoSeal™ VCS-iga koos tarnitava 0,038-tollise juhtetraadi kliinilise kasutamise ohutuse ja toimivusega. Uuringu küsimused keskendusid eeskätt juhtetraadi üldisele kasutamisele alates vaskulatuuri sisestamisest läbi protseduurikanüüli kuni traadi eemaldamiseni.

FemoSeal™ VCS ja seadmega kaasas olev 0,038-tolline juhtetraat said vastuvõetavad hinnangud, seadme kohta esitati kuus (6) kaebust ja juhtetraadi kohta üheksa (9) muud teadet, lähtuvalt kõrge kvaliteediga kliinilistest uuringutest saadud arvamuste hindamisest. Kaebusi FemoSeali kui ka juhtetraadi suhtes on hinnatud ning neid hinnati Terumo turustamisjärgse järelevalve toimingute raames. Tuvastatud ei ole uusi riske ega riskitasemeid.

2024. aastal viidi PMCF-tegevuste raames läbi arstide kasutajaküsitlus. Uuringu tulemused näitasid, et FemoSeal™ VCS-i toimivuse ja ohutuse hinnang oli üldiselt väga soodne. Näidati ka teiste juhtetraatide ühilduvust peale FemoSeal™ VCS-iga kaasasoleva standardi.

#### **1.4.3.2 Käimasolev/kavandatav turustamisjärgne kliiniline järelkontroll**

TMC-l on käimas/kavas kaks turustamisjärgset järelkontrolli toimingut. Läbi viiakse kliiniline küsitlus, et koguda prospektiivselt tagasisidet seoses juhtetraadi kasutamisega, mida müüakse koos EL-i turul oleva FemoSeal VCS-iga. Küsimustiku täidavad arstid, et oleks võimalik uurida, milliseid juhtetraate nad protseduuri käigus kasutasid. Selle uuringu eesmärk on kõrvaldada lünk, mis on tuvastatud kirjanduse ja kommentaaride puudumise tõttu FemoSeal™ VCS-i ühilduvuse kohta teiste mitte-Terumo kaubamärkide juhtetraatidega. Tagasiside sisaldab tehnilisi tulemusi, kliinilist toimivust ja ohutust seoses seadme toimimisega koos erinevate juhtetraatidega.

#### **1.4.4 Süstemaatilise kirjanduse ülevaate andmete kokkuvõte**

Terumo Medical Corporation viib läbi süstemaatilisi kirjanduse ülevaateid, et koguda ja hinnata kliinilisi ohutus- ja toimivusandmeid vaskulaarse sulgemisseadme FemoSeal™ VCS ja/või sarnaste seadmete kohta avaldatud uuringutest. Avaldatud kirjanduse iga-aastase läbivaatuse eesmärk on tuvastada varem teadmata kõrvaltoimed, jälgida teadaolevaid kõrvaltoimeid, tuvastada tekkivad riskid ja teha kindlaks FemoSeal™ VCS-i võimalik süstemaatiline väärkasutus või näidustuseväline kasutamine.

Viimases süstemaatilises kirjanduse ülevaates, mis hõlmas ajavahemikku 1. septembrist 2019 kuni 31. augustini 2024, tuvastati 29 avaldatud uuringut, mis andsid kliinilisi ohutus- ja toimivusandmeid FemoSeal™ VCS-i kohta. Üheksas uuringus teatati 23 viitest FemoSeal™



VCS-i ettenähtud ja ka mitteettenähtud kasutamisele. FemoSeal™ VCS-i kasutamist vaatlevate uuringute kirjanduse ülevaade kirjeldas uuritavat populatsiooni, mis vastas EL-is perkutaanseid vaskulaarseid kateteriseerimisprotseduure läbivatele patsientidele. Nende 23 eelretsenseeritud publikatsiooni nimekirja vt **jaotisest 3**.

Kliinilist toimivust hinnati järgmiste meetoditega.

- Hemostaasi aeg on parem kui reiearteri perkutaanse sulgemise tehnika nüüdistase või sellega samaväärne.
- Liikumahakkamisele kuluv aeg on parem kui reiearteri perkutaanse sulgemise tehnika nüüdistaseme korral või sellega samaväärne.
- Operatsioonijärgsete tüsistuste määr on võrreldav või väiksem kui praegustes ravistandardites.

Nende kliiniliste jõudlusandmete põhjal näitasid selles kirjanduse ülevaates esitatud andmed, et FemoSeal™ VCS-i võib edukalt kasutada reiearteri punktsiooni (arteriotoomia) sulgemiseks patsientidel, kes on läbinud 7 Fr või väiksema protseduurikanüüliga perkutaanse kateteriseerimise protseduuri. Täielik hemostaas saavutati enamikul patsientidest (79,65-100% juhtudest) ja see oli seotud hemostaasi saavutamise aja mediaaniga 0,5 min, keskmine aeg väljakirjutamiseni 3 päeva. 69,2-86,7% patsientidest suutis 5 tundi pärast sooneava sulgemist kõndida, keskmine operatsioonijärgne voodiaeg oli 349 min. FemoSeal™ VCS-i rike esines 3,68-4% juhtudest ja 0,9-4,4% protseduuride puhul oli vaja täiendavat manuaalset kompressiooni.

Kliinilist ohutust hinnati kõrvalnähtude alusel, mille hulka kuulusid mh, aga mitte üksnes järgmised kõrvalnähud.

- Veritsus
- Hematoom
- Pseudoaneurüsm
- Verevalum
- Arteriovenoosne fistul
- Infektsioon
- Surm

Hõlmatud uuringutes oli kõigi FemoSeal™ VCS-iga seoses teatatud kõrvalnähtude esinemissagedus madalam kui varem manuaalse kompressiooni ja muude vaskulaarsete sulgemisseadmetega seoses teatatud määrad või nendega võrreldav.

10 juhtumiuuringu läbivaatamisel ei tuvastatud ühtegi kõrvalnähtu, kuna uusi, ootamatuid, esilekerkivaid ega vastuvõetamatuid riske ei tuvastatud.

FemoSeal™ VCS-i kasutamise üldine tõhusus diagnostilise angiograafia või interventsionaalsete operatsioonide ajal sõltub mitmetest teguritest, nagu sugu, vanus, patsiendi anatoomia, kaasuvad haigused, punktsioonikoha anatoomiline asukoht, kirurgi kogemus, VCD paigaldusmeetod, operatsioonijärgne hooldus jne. Lisaks tehnilisele edule, sh hemostaasi saavutamisele, pakkus FemoSeal™ VCS kliinilist kasu vaskulaarse sulgemise korral pärast reiearteri punktsiooni, näiteks hemostaasini kuluva aja ja liikumahakkamiseni kuluva aja lühendamist. FemoSeal™ VCS-i toimivusnäitajad on kooskõlas selle seadmetüübi eeldatavate tulemustega, kui seda kasutatakse ettenähtud viisil. Mõned praeguse otsinguperioodi jooksul leitud viited näitasid, et uuritavat seadet kasutati muus anatoomilises asukohas kui ühisreiearteris ja > 7 Fr arteriotoomiate sulgemiseks, mida loetakse mitteettenähtud kasutuseks.

Ülevaatus käigus ei tuvastatud teadmata kõrvaltoimeid, uusi riske ega seadme võimalikku süstemaatilist väärkasutust. Kui FemoSeal™ VCS-i kasutavad väljaõppinud arstid ettevaatlikult, toimib meditsiiniseade siiski kasuliku ja vajaliku kliinilise seadmena. Üldiselt rahuldab sihtravi ja seega FemoSeal™ VCS praegust kliinilist vajadust vaskulaarse juurdepääsuga seotud tüsistuste ravis.

Selles kirjanduse ülevaates esitatud andmete põhjal ei tuvastatud kliinilistes tingimustes ühtki toimivus- ega ohutusprobleemi, mis oleks olnud varem teadmata, ega kõrvaltoimeid, mis oleks ilmnenud oodatust/vastuvõetavast suuremal määral. Seetõttu võib kirjanduse ülevaatest järeldada, et FemoSeal™ VCS, mida kasutatakse hemostaasi saavutamiseks arteriotoomia paikmes pärast perkutaanset kateteriseerimist, töötab eeldatud viisil ega seostu tõsiste kõrvaltoimetega.

#### 1.4.5 Turustamisjärgsete uuringute andmete kokkuvõte

Kehtestatud on ennetav PMS-süsteem ning kõikide kaebuste läbivaatamine toimub iga kuu ja kooskõlas ettevõttesiseste tootmisprotseduuridega. Kaebuste andmeid analüüsiti ajavahemikus 1. septembrist 2019 kuni 31. augustini 2024. Kokku esitati tootjale 28 meditsiiniseadme järelevalveteatist (MDV) ja 476 kliendikaebuste teatist. 28-st MDV teatest 27 olid seotud kõrvaltoimetega ja üks seadme talitlushäirega. Aruandeperioodil esines kaks surmajuhtumit, kuid ükski teatatud surmajuhtum ei olnud seotud uuritava seadmega. Tootjale esitatud 476 kaebuse seas olid kõige sagedasemad kaebuste põhjused paigaldusraskused (146 juhtu, 0,0142% esinemissagedus). Väljatõmbetõrked olid sageduselt teine, esinemissagedus 0,0126% (130 juhtu).

FemoSeal™-i vaskulaarse sulgemise süsteemion üle kogu maailma müüdud üle 1 033 136 ja Euroopa Majanduspiirkonnas 827 843. Ülemaailmse müügi alusel on kaebuste arvutuslik sagedus 0,046%. Kliendikaebuste üldine määr on väga madal. Ei tuvastatud uusi riske, mida ei oleks käsitletud kasutusjuhendis ja riskidokumentatsioonis.

Kõrvaltoimete esinemissagedused on esitatud **tabelis 1.2**. Ühtegi uut ettenägematut, esilekerkivat ega vastuvõetamatut riski ei tuvastatud. Teadaolevate kõrvaltoimete esinemissagedus või raskusaste ei suurenenud oluliselt.

#### 1.4.6 Kliinilise toimivuse ja ohutuse üldkokkuvõte

FemoSeal™ VCS on ette nähtud kasutamiseks ühisreiearteri punktsioonikoha (arteriotoomia) sulgemiseks patsientidel, kellele on tehtud perkutaanne kateteriseerimine 7 Fr (2,33 mm) või väiksema protseduurikanüüliga. See kliiniline hindamine põhineb FemoSeal™ VCS-i kavandatud kasutust puudutavate kättesaadavate turustamiseelsete ja turustamisjärgsete kliiniliste andmete ning kirjanduse põhjalikul analüüsil.

Avaldatud kirjanduse põhjalik ülevaatus hõlmas ajavahemikku 1. septembrist 2019 kuni 31. augustini 2024. Tõendusmaterjali hulka kuulus 29 uuringut FemoSeal™ VCS-i kohta. Kliinilises hindamises esitatud tõendid viivad järeldusele, et näidatud viisil kasutamisel on uuritav seade ohutu ja efektiivne ning kõik riskid või soovimatud kõrvaltoimed, mis võivad seadmega tavapärastes kasutustingimustes kaasneda, on võrdluses patsiendile avalduva kasuga vastuvõetavad riskid. Katsealuste seadmete toimivusnäitajad on kooskõlas selle seadmetüübi eeldatavate tulemustega, kui seda kasutatakse ettenähtud viisil.

FemoSeal™ VCS-i kasutamisega seotud võimalikud kõrvaltoimed hõlmavad ka teiste arteriotoomia sulgemise meetoditega seoses sageli teatatud kõrvalnähtusid, näiteks veritsust ja hematoomi. Üldiselt sarnanesid FemoSeal™ VCS-i kasutamisega teatatud kõrvalnähtude esinemissagedused manuaalse kompressiooni ja sarnaste vaskulaarsete sulgemisseadmete kasutamisel teatatud sagedustega. Täpsemalt on FemoSeal™ VCS-iga seoses teatatud veritsuse ja hematoomide määrad madalamad kui sarnaste veresoone sulgemisseadmetega seoses teatatud määrad. Kõik teatatud kõrvalnähtud, nii avaldatud kirjandusest kui ka turustamisjärgsest järelevalvest pärinevad, olid eelnevalt tuvastatud (vt **lõik 1.3**).

Olemasolevad andmed FemoSeal VCS-i kliinilise ohutuse ja efektiivsuse kohta näitavad, et patsiendi saadav kasu selle vaskulaarse sulgemisseadme kasutamisel kaalub üles võimalikud riskid, kui seda kasutatakse kasutusjuhendi kohaselt.

Nagu eelmistes jaotistes märgitud, näitavad FemoSeal™ VCS-i kohta esitatud andmed vastavust hinnatava seadmega seotud andmete (nt seadme kasutamine, ohutuse tulemused, kliiniline toimivus ja kliiniline kasu), identifitseeritud samaväärsete seadmete ja sarnaste seadmetega seotud andmete vahel, mis on loetletud tehnika nüüdisaegse taseme kirjelduses.

Ohutusandmete ristanalüüsis ei tuvastatud lünki järgmiste andmete vahel:

- Tehnika nüüdistaseme kirjelduses nimetatud andmed
- Hinnatava seadme spetsiifilised andmed
- Riskijuhtimise dokumentatsioonis nimetatud andmed
- Märgistuses ja/või kasutusjuhendis nimetatud andmed (st käsitletakse kasutajale edasiantavaid jääkriske).

Kliiniline ohutus on tõendatud tüsistuste väikese esinemissagedusega, mis on tuvastatud avaldatud eelretsenseeritud kliinilises kirjanduses, ettevõtte spondeeritud kliinilistes uuringutes ja turuletoomisjärgsete andmete läbivaatamisel ning lisaks turult tagasivõtmiste puudumisega. Toimivusega seotud probleeme ei ole tuvastatud, läbivaadatud kirjandus sisaldas FemoSeal™ VCS-i kasutamist kooskõlas tootja kavandatud kasutusviisiga.

### **1.5 Võimalikud alternatiivsed diagnostika- või ravivõimalused**

Traditsiooniliselt kasutatakse pärast vaskulaarset kateteriseerimist hemostaasi saavutamiseks arteriotoomiakohal manuaalset kompressiooni. Manuaalse kompressiooni korral on patsient pikka aega immobiilne (kuni 8 tundi pärast protseduuri) ning sellega kaasneb oluline ebamugavustunne ja pikk haiglasviibimine. Hiljutises süstemaatilises ülevaates leiti, et mediaanaeg hemostaasi saavutamiseni manuaalse kompressiooni korral on 20,8 minutit.

Alternatiivid manuaalsele kompressioonile on välised hemostaatilised seadmed, mis avaldavad arteriotoomiakohale mehaanilist survet. Need seadmed ei lühenda aega hemostaasini ega liikumahakkamiseni, vaid vähendavad personalivajadust, asendades manuaalse kompressiooni mehaanilise survega. Mehaanilise kompressiooni kasutamisega seotud kõrvalnähtude määrad sarnanevad manuaalse kompressiooni kasutamisele.

Veresoonte sulgemisseadmed, nagu FemoSeal™ VCS, on ette nähtud arteriotoomia sulgemiseks. Nende eesmärk on vähendada aega hemostaasini ja teha võimalikuks varasem liikuma hakkamine. Hiljuti läbi viidud süstemaatilises ülevaates 13 kaubandusvõrgus saadaoleva seadmega leiti, et mediaanaeg hemostaasi saavutamiseni vaskulaarse sulgemisseadmega on 5,4 minutit. Kõigi vaskulaarsete sulgemisseadmete mediaanne hemostaasiaeg on vahemikus 1 minut (FemoSeal™ VCS) kuni 14 minutit; enamasti 4 kuni 10 minutit.<sup>1</sup>

Arteriotoomiakoha sulgemisega seotud sageli teatatud kõrvalnähud manuaalse kompressiooni, välise hemostaasiseadmete või vaskulaarsete sulgemisseadmete kasutamisel on muu hulgas hematoom, veritsus ligipääsukohas, pseudoaneurüsm, arteriovenoosne fistul ja infektsioon. Sama süstemaatiline ülevaade (34 randomiseeritud kontrollitud uuringut, 14 401 patsienti) leidis, et kõrvaltoimete esinemissagedus oli manuaalse kompressiooni ja vaskulaarsete sulgemisseadmete kasutamisel sarnane, välja arvatud veritsuse osas, mis kaldus vaskulaarsete sulgemisseadmete puhul olema veidi kõrgem.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Soovitatav kasutajaprofiil ja väljaõpe

FemoSeal™ Vascular Closure Systemi ettenähtud kasutajad on arstid, kes on saanud väljaõppe arteriaalse ligipääsu ja sulgemisega endovaskulaarseteks protseduurideks ühisreiarteri kaudu ning kes on osalenud Terumo Medical Corporationi FemoSeal™-i arstide väljaõppeprogrammis.

## 1.7 Asjakohased ühtlustatud ja ühised standardid

| Standardi number | Praegune vastavusaasta / versioon | Kirjeldus                                                                                                                                |
|------------------|-----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070        | 2014/AMD1:2018                    | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070     | 2014/A1:2018                      | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance     | 20. mai 2021                      | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052       | 2015                              | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213       | 2017                              | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503       | 2020                              | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182       | 2019                              | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |
| EN ISO 13485     | 2016/A11:2021                     | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 13485        | 2016                              | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |

| Standardi number | Praegune vastavusaasta / versioon | Kirjeldus                                                                                                                                                                |
|------------------|-----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14644-1      | 2015                              | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1   | 2015                              | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2      | 2015                              | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2   | 2015                              | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3      | 2019                              | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3   | 2019                              | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1      | 2003                              | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1   | 2003                              | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2      | 2003/TC1:2004                     | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| EN ISO 14698-2   | 2003/TC 1:2004                    | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| USP <788>        | N/A                               | PARTICULATE MATTER IN INJECTIONS                                                                                                                                         |

| Standardi number       | Praegune vastavusaasta / versioon | Kirjeldus                                                                                                            |
|------------------------|-----------------------------------|----------------------------------------------------------------------------------------------------------------------|
| EU Pharmacopeia 2.9.19 | N/A                               | Particulate Contamination: Sub-Visible Particles                                                                     |
| IEC 62366-1            | 2015                              | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN 62366-1             | 2015                              | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN ISO 14971           | 2019/A11:2021                     | Medical devices — Application of risk management to Medical devices                                                  |
| ISO 14971              | 2019                              | Medical devices — Application of risk management to Medical devices                                                  |
| ASTM F1980             | 2016                              | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1         | 2020                              | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1            | 2018                              | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2         | 2006                              | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2            | 2006                              | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3         | 2014                              | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3            | 2014                              | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4         | 2017                              | Biological Evaluation of Medical Devices — Part 4: Selection of tests for interactions with blood                    |

| Standardi number | Praegune vastavusaasta / versioon | Kirjeldus                                                                                                      |
|------------------|-----------------------------------|----------------------------------------------------------------------------------------------------------------|
| ISO 10993-4      | 2017                              | Biological Evaluation of Medical Devices — Part 4: Selection of tests for interactions with blood              |
| EN ISO 10993-5   | 2009                              | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                             |
| ISO 10993-5      | 2009                              | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                             |
| EN ISO 10993-6   | 2016                              | Biological evaluation of medical devices – Part 6: Tests for local effects after implantation                  |
| ISO 10993-6      | 2016                              | Biological evaluation of medical devices – Part 6: Tests for local effects after implantation                  |
| EN ISO 10993-10  | 2023                              | Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization                |
| ISO 10993-10     | 2021                              | Biological evaluation of medical devices — Part 10: Tests for irritation and skin sensitization                |
| EN ISO 10993-11  | 2018                              | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                |
| ISO 10993-11     | 2017                              | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                |
| EN ISO 10993-12  | 2021                              | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                 |
| ISO 10993-12     | 2021                              | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                 |
| EN ISO 10993-17  | 2009                              | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances |
| ISO 10993-17     | 2002                              | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances |



| Standardi number | Praegune vastavusaasta / versioon | Kirjeldus                                                                                                                                                                    |
|------------------|-----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-18     | 2020/A1:2022                      | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-18  | 2020/A1:2022                      | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-23  | 2021                              | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23     | 2021                              | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382       | 2018                              | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756        | 2017                              | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>         | N/A                               | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>        | N/A                               | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72   | 2019                              | Bacterial endotoxins – Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135     | 2014/A1:2019                      | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135        | 2014/A1:2018                      | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |

| Standardi number | Praegune vastavusaasta / versioon | Kirjeldus                                                                                                                                                       |
|------------------|-----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-7   | 2008/A1:2022                      | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                       |
| ISO 10993-7      | 2008/A1:2019                      | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                               |
| EN 556-1         | 2024                              | Sterilization of medical devices – Requirements for medical devices to be designated "STERILE" – Part 1: Requirements for terminally sterilized medical devices |
| EN ISO 11737-1   | 2018/A1:2021                      | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11737-1      | 2018/A1:2021                      | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| EN ISO 11138-1   | 2017                              | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-1      | 2017                              | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| EN ISO 11138-2   | 2017                              | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 11138-2      | 2017                              | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| EN ISO 15223-1   | 2016                              | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| ISO 15223-1      | 2016                              | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| EN 1041          | 2008/A1:2013                      | Information supplied by the manufacturer of medical devices                                                                                                     |

| Standardi number  | Praegune vastavusaasta / versioon | Kirjeldus                                                                                                                                                                  |
|-------------------|-----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 11607-1    | 2020/A1:2023                      | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| ISO 11607-1       | 2019/A1:2023                      | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| EN ISO 11607-2    | 2020/A1:2023                      | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ISO 11607-2       | 2019/A1:2023                      | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169        | 2016                              | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M | 2016                              | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825        | 2018                              | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096        | 2011 (R 2019)                     | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M     | 2015                              | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24      | 2021                              | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3       | 2020                              | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |

| Standardi number | Praegune vastavusaasta / versioon | Kirjeldus                                                                                                                                                                                          |
|------------------|-----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-8      | 2020                              | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                                                     |
| MDCG 2020-7      | 2020                              | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                                                  |
| MDCG 2020-6      | 2020                              | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                                               |
| MDCG 2019-9 v1   | 2022                              | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                           |
| MDCG 2019-8 v2   | 2020                              | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                 |
| MDCG 2020-15     | 2020                              | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                           |
| MDCG 2021-11     | 2021                              | Guidance on Implant Card – ‘Device types’                                                                                                                                                          |
| MDCG 2021-19     | 2021                              | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                            |
| MDCG 2018-1 v4   | 2021                              | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                     |
| MDCG 2019-2      | 2019                              | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                 |
| MDCG 2019-1      | 2019                              | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                 |
| MDCG 2018-7      | 2018                              | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro |

| Standardi number    | Praegune vastavusaasta / versioon | Kirjeldus                                                                                                                                                                                     |
|---------------------|-----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                     |                                   | Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR))                                                                                                                                    |
| MDCG 2018-6         | 2018                              | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746   |
| MDCG 2018-4         | 2018                              | MDCG 2018-4 Annex: UDI database Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                                  |
| MDCG 2018-3 v1      | 2020                              | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25        | 2021                              | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2.12-2 Rev 2 | 2012                              | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                        |

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### 3.0 MUUDATUSTE AJALUGU

| SSCP versiooni number      | Väljaandmiskuupäev | Muudatuse kirjeldus                                                           | Teavitatud asutuse valideeritud versioon                                                                                                                                                                                                                                                                                                            |
|----------------------------|--------------------|-------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022               | 20. jaanuar 2023   | Esimene väljaanne, MDR-i CE-sertifikaadiga                                    | <p><input checked="" type="checkbox"/> Jah</p> <p>Valideerimiskeel: English</p> <p><input type="checkbox"/> Ei (kehtib ainult klass IIa või teatud IIb implanteeritavate seadmete kohta (MDR, artikkel 52 (4) 2. lõik), mille puhul teavitatud asutus ei ole veel SSCP-d valideerinud)</p> <p><input type="checkbox"/> Muu (palun täpsustage):</p>  |
| SSCP-FS-2023 – 1. versioon | 15. märts 2024     | Uuendatud andmetega ajavahemikust 1. jaanuar 2019 kuni 31. detsember 2023     | <p><input checked="" type="checkbox"/> Jah</p> <p>Valideerimiskeel: English</p> <p><input type="checkbox"/> Ei (kehtib ainult IIa või teatud IIb klassi implanteeritavate seadmete kohta (MDR, artikkel 52 (4) 2. lõik), mille puhul teavitatud asutus ei ole veel SSCP-d valideerinud)</p> <p><input type="checkbox"/> Muu (palun täpsustage):</p> |
| SSCP-FS-2023<br>Versioon 1 |                    | Uuendatud andmetega ajavahemikust 1. septembrist 2019 kuni 31. augustini 2024 | <p><input type="checkbox"/> Jah</p> <p>Valideerimiskeel: English</p> <p><input type="checkbox"/> Ei (kehtib ainult IIa või teatud IIb klassi implanteeritavate seadmete kohta (MDR, artikkel 52 (4) 2. lõik), mille puhul teavitatud asutus ei ole veel SSCP-d valideerinud)</p> <p><input type="checkbox"/> Muu (palun täpsustage):</p>            |

|                           |               |                                                           |                                                                                                                                                                                                                                                                                                                                                            |
|---------------------------|---------------|-----------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2023<br>Version 2 | June 20, 2025 | Läbi vaadatud NSAI<br>päringute põhjal<br>valideerimiseks | <input checked="" type="checkbox"/> Jah<br>Valideerimiskeel: English<br><br><input type="checkbox"/> Ei (kehtib ainult IIa või<br>teatud IIb klassi<br>implanteeritavate seadmete<br>kohta (MDR, artikkel 52 (4) 2.<br>lõik), mille puhul teavitatud<br>asutus ei ole veel SSCP-d<br>valideerinud)<br><br><input type="checkbox"/> Muu (palun täpsustage): |
|---------------------------|---------------|-----------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

## TURVALLISUUTTA JA KLIINISTÄ SUORITUSKYKYÄ KOSKEVA TIIVISTELMÄ

### FemoSeal™ Vascular Closure System

|                                                                          |                                                                                              |
|--------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|
| <b>Valmistaja</b>                                                        | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 USA          |
| <b>Valmistajan SRN</b>                                                   | US-MF-000019594                                                                              |
| <b>Johdon edustaja / säännösten<br/>noudattamisesta vastaava henkilö</b> | Kimberly Feitl<br>Vice President, Quality                                                    |
| <b>Basic UDI-DI</b>                                                      | 38970FS79                                                                                    |
| <b>EMDN-numero</b>                                                       | C900199 – Hemostaasijärjestelmät – Muut                                                      |
| <b>Laiteluokka</b>                                                       | Luokka III                                                                                   |
| <b>Laitteen ensimmäinen<br/>CE-merkintävuosi</b>                         | 2005                                                                                         |
| <b>EU:n valtuutettu edustaja</b>                                         | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgium<br>SRN: BE-AR-000001433 |
| <b>Ilmoitettu laitos</b>                                                 | NSAI<br>CE 0050                                                                              |

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Tämän turvallisuutta ja kliinistä suorituskyyä koskevan tiivistelmän (Summary of Safety and Clinical Performance, SSCP) tarkoituksena on mahdollistaa julkinen pääsy FemoSeal™ Vascular Closure Systemin (VCS) turvallisuuteen ja kliiniseen suorituskyyyn liittyvien keskeisten seikkojen päivitettyyn tiivistelmään.

Käyttäjille / terveydenhuollon ammattihenkilöille tarkoitettu tiivistelmä laitteen turvallisuudesta ja kliinisestä suorituskyyvystä on alla **kohdassa 1.0**.

## **1.0 TIIVISTELMÄ KÄYTTÄJILLE / TERVEYDENHUOLLON AMMATTIHENKILÖILLE**

SSCP:n ei ole tarkoitus korvata käyttöohjetta pääasiallisena asiakirjana laitteen turvallisen käytön varmistamiseksi, eikä sen ole tarkoitus antaa diagnostisia tai hoitoa koskevia ehdotuksia käyttötarkoituksen mukaisille käyttäjille tai potilaille. SSCP:tä ei ole tarkoitettu korvaamaan implanttikorteissa tai muissa pakollisissa asiakirjoissa olevia pakollisia tietoja.

### **1.1 Laitteen käyttötarkoitus**

#### **1.1.1 Käyttötarkoitus**

FemoSeal™ Vascular Closure System on lääkinällinen laite, joka on tarkoitettu valtimopunktion sulkemiseen yhteisen reisivaltimon kautta suoritettun perkutaanisen katetroinnin jälkeen.

#### **1.1.2 Käyttöindikaatiot**

FemoSeal™ Vascular Closure System on tarkoitettu yhteisen reisivaltimon punktion (arteriotomian) sulkemiseen potilailla, joille on suoritettu perkutaaninen katetrointi käyttämällä enintään 7F (2,33 mm) -kokoista toimenpideholkkia.

#### **1.1.3 Vasta-aiheet ja/tai rajoitukset**

FemoSeal™ Vascular Closure System on vasta-aiheinen potilailla, joiden arteriotomiassa on käytetty yli 7F:n (2.33 mm) holkkeja tai laitteita.

#### **1.1.4 Kohdepotilasryhmät**

FemoSeal™ Vascular Closure Systemin turvallisuus ja teho on varmistettu vähintään 18-vuotiailla potilailla, joille on suoritettu perkutaaninen katetrointi käyttäen enintään 7F (2,33 mm) -kokoista toimenpideholkkia.

#### **1.1.5 Erityispotilasryhmät**

FemoSeal™ Vascular Closure Systemin turvallisuutta ja tehoa ei ole varmistettu seuraavissa potilasryhmissä:

- Potilaat, joilla on autoimmuunisairaus.
- Potilaat, jotka saavat trombolyyssihoitoa.
- Potilaat, joilla on kliinisesti merkittävä ääreisverisuonisairaus.
- Potilaat, joilla on hoitamaton hypertensio (systole > 220 mmHg tai diastole > 110 mmHg).
- Potilaat, joilla on verenvuotohäiriö, mukaan lukien trombositopenia (verihiutalearvo < 100 000) tai anemia (Hgb < 10 mg/dl).
- Potilaat, joiden yhteisen reisivaltimon sisälumen on alle 5 mm.

- Potilaat, joilla on munuaisten ja/tai maksan vajaatoiminta.
- Potilaat, joilla on muita merkittäviä samanaikaisia sairauksia.
- Tiettyä rotua ja/tai etnistä alkuperää edustava populaatio.
- Potilaat, joilla on ollut sydäninfarkti 72 tunnin kuluessa.
- Potilaat, joilla on verisuonisiirre tai stentti punktiokohdassa.
- Potilaat, jotka ovat raskaana tai imettävät.
- Alle 18-vuotiaat potilaat.

### 1.1.6 Suunnitellut käyttäjät

FemoSeal™ Vascular Closure Systemin suunnitellut käyttäjät ovat lääkäreitä, joilla on koulutus valtimoyhteyden avaamiseen ja sulkemiseen endovaskulaarisissa toimenpiteissä yhteisen reisivaltimon kautta ja jotka ovat osallistuneet Terumo Medical Corporationin lääkäreille tarkoitettuun FemoSeal™-opetusohjelmaan.

## 1.2 Laitteen kuvaus

### 1.2.1 Laitteen kuvaus

Terumo Medical Corporationin (TMC) valmistama FemoSeal™ Vascular Closure System on resorboituva verisuonensulkulaite, joka on tarkoitettu reisivaltimon hemostaasin aikaansaamiseen perkutaanisen katetroinnin jälkeen yhteisen reisivaltimon kautta.

FemoSeal™-laitteen sulkuelementit koostuvat kahdesta resorboituvasta polymeerilevystä, sisätiivisteestä ja ulkoisesta lukituslevystä, jotka kiinnittyvät yhteen resorboituvalla monisäikeisellä langalla sulkien näin arteriotomian mekaanisesti (katso **kuva 1.1** ja **kuva 1.2**). Kun ulkoinen lukituslevy on viety kartioholkin läpi, se työnnetään monisäikeisen langan sisältävään akseliin, jolloin punktiokohta sulkeutuu mekaanisesti sisemmän ja ulomman lukituslevyn väliin. Sisätiiviste ja ulkoinen lukituslevy pysyvät paikallaan monisäikeisen langan sisältävän akselin kitkan avulla. Hemostaasi saavutetaan mekaanisin keinoin. Sulkuelementit hajoavat hydrolyysin kautta.

Implantoitavat sulkukomponentit, sisätiiviste ja ulkoinen lukituslevy, hajoavat kahdeksassatoista (18) kuukaudessa, kun taas monisäikeisen langan arvioidaan hajoavan ja resorboituvan ympäröivän kudoksen hydrolyysin kautta 2–3 vuoden kuluessa. Implantoitavien sulkukomponenttien on testattu säilyttävän kompression arteriotomiakohdassa enintään kahdeksan (8) tunnin ajan. Hajoamistuotteet metaboloituvat ja erittyvät virtsaan tai poistuvat hiilidioksidina keuhkojen kautta. Eläinkokeissa ei ole havaittu kertymistä. Muut FemoSeal™-laitteen osat, jotka

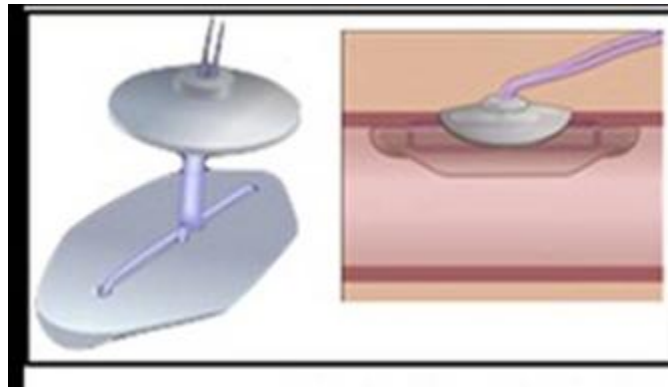


joutuvat kosketuksiin elävän kudoksen tai veren kanssa toimenpiteen aikana, ovat kartioholkki, laajennin, työntöputki, työnnin ja johdin.

**Kuva 1.1 Sisätiiviste ja ulkoinen lukituslevy**

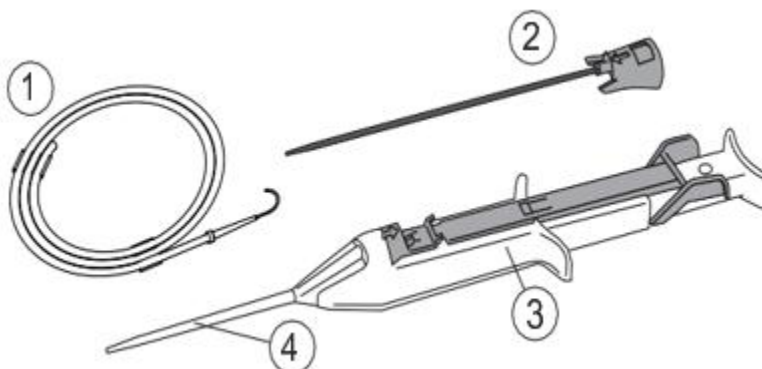


**Kuva 1.2 Sisätiiviste ja ulkoinen lukituslevy aktivoituna**



FemoSeal™-yksikön pakkauksessa on lisäksi laajennin, 70 cm (27,5") pitkä johdin, jonka ulkoläpimitta on 0,038" (0,97 mm), ja J-suoristaja, katso **kuva 1.3** alla. Johdin on polyeteeniletkun sisällä. Kaikki osat on pakattu kiinteälle paperialustalle. Pakkaus sisältää myös potilaan implanttikortin. FemoSeal™ Vascular Closure System ei vaadi lisätarvikkeita, jotta laite toimisi tarkoitetulla tavalla, ja laite on tarkoitettu käytettäväksi vain tuotteen pakkauksessa olevan laajentimen ja johtimen kanssa.

**Kuva 1.3 FemoSeal™ VCS -yksikkö, johdin ja laajennin**



## 1.2.2 Raaka-aineet ja komponentit

Taulukossa 1.1 alla luetellaan FemoSeal™ VCS:n komponentit.

**Table 1.1 FemoSeal™ VCS:n raaka-aineet ja komponentit**

| Osanumero | Kuvaus                                 |                                                                 | Materiaalit                                                                                                                                                                    |
|-----------|----------------------------------------|-----------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1         | 0,038" (0,97 mm) johdin ja J-suoristin |                                                                 | Johdin: 304 ruostumaton teräs<br>J-suoristin: Polypropeeni, sinipunainen pigmentti<br>Pidike: Polyeteeni<br>Letku: Polyeteeni                                                  |
| 2         | FemoSeal-laajennin                     |                                                                 | Kanta: Tetrahydrofuraani, sininen pigmentti, polybuteenitereftalaatti (PBT)<br>Putki: Suuritiheyspolyeteeni (PE-HD), musta pigmentti<br>Voiteluaine: Silikoni, Dow Corning 360 |
| 3/4       | FemoSeal-yksikkö                       | Muottiin puristettu RD7 – Sisätiiviste ja ulkoinen lukituslevy* | Glykolidin, trimetyleenikarbonaatin, ε-kaprolaktonin kopolymeeri ja TMP: trimetylolipropaani (initiaattori)                                                                    |
|           |                                        | Monisäikeinen lanka*                                            | L, L-laktidin, trimetyleenikarbonaatin, ε-kaprolaktonin segmentoitu kopolymeeri ja 1,3-propaanidioli (initiaattori)                                                            |

|  |  |                  |                                                                   |
|--|--|------------------|-------------------------------------------------------------------|
|  |  |                  | Pinnoite on glykolidin, ε-kaprolaktonin ja L-lysiinin kopolymeeri |
|  |  | Työntöputki      | Polypropeeni                                                      |
|  |  | Työnnin          | 304V ruostumaton teräs                                            |
|  |  | Liukukytin       | Polybuteenitereftalaatti (PBT)                                    |
|  |  | Kotelo           | Polybuteenitereftalaatti (PBT)                                    |
|  |  | Painike          | Polybuteenitereftalaatti (PBT)                                    |
|  |  | Painikkeen kansi | Polyoksimetyyleeni (POM)/polyasetaaali-kopolymeeri                |
|  |  | Holkki           | Polybuteenitereftalaatti (PBT)                                    |
|  |  | Välilevy         | Polybuteenitereftalaatti (PBT)                                    |
|  |  | Kartio           | Polypropeeni                                                      |
|  |  | Kotelon kansi    | Polybuteenitereftalaatti (PBT)                                    |
|  |  | Turvasalpa       | Polybuteenitereftalaatti (PBT), sininen pigmentti                 |
|  |  | Holkin kansi     | Polybuteenitereftalaatti (PBT)                                    |
|  |  | Letkun tiiviste  | Silikoni, lujuus A 70                                             |
|  |  | Kotelon tiiviste | Silikoni, lujuus A 50                                             |
|  |  | Jousi            | 302 ruostumaton teräs                                             |
|  |  | Kartioholkki     | Polypropeeni<br>Silikoni Dow Corning 360, heksaani                |

\* Laitteen implantoitava osa: implantoitavat osat ovat MRI-turvallisia

FemoSeal™ VCS on steriloitu eteenioksidilla (EO), ja se on kertakäyttöinen lääkinällinen laite. FemoSeal™ VCS -laite on suunniteltu siten, ettei sitä voi käyttää uudelleen.

### **Toimintatapa**

FemoSeal™ VCS saa aikaan hemostaasin mekaanisesti aktivoimalla implantoitavat sulkuelementit yhteisen reisivaltimon sisä- ja ulkopuolella. Verenvuodon estävä mekanismi koostuu sisätiivisteestä, joka tiivistää punktiokohdan, ja ulkoisesta lukituslevystä, joka pitää sisätiivisteen paikallaan.

### 1.2.3 Kliiniset hyödyt

FemoSeal™ VCS antaa seuraavat kliiniset hyödyt verrattuna suonon sulkemiseen yhteisen reisivaltimon punktion jälkeen:

- Nopeampi hemostaasi<sup>1</sup>
- Potilas pääsee nopeammin liikkumaan<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

### 1.2.4 Aiemmat laitesukupolvet tai variantit

- FemoSeal™ VCS:n (#11200) ensimmäistä versiota myytiin Euroopan markkinoilla vuonna 2005 ja osan vuotta 2006.
- Nykyinen FemoSeal™ VCS (#11202), jonka toimitusjärjestelmää on parannettu, on ollut markkinoilla 28.3.2006 lähtien.

### 1.2.5 Laitteen kanssa käytettäväksi tarkoitetut lisävarusteet

FemoSeal™-yksikön pakkauksessa on lisäksi laajennin, 70 cm (27,5") pitkä johdin, jonka ulkoläpimitta on 0,038" (0,97 mm), ja J-suoristaja. Johdin on FemoSeal™-yksikön lisävaruste. J-suoristaja on johtimen osa, kun taas laajennin on FemoSeal™-yksikön osa. Johdin on ainoa tarvittava lisävaruste. Johdin on polyteeniletkun sisällä. Kaikki osat on pakattu kiinteälle paperialustalle. Pakkaus sisältää myös potilaan implanttikortin. FemoSeal™ Vascular Closure System ei vaadi lisätarvikkeita, jotta laite toimisi tarkoitetulla tavalla, ja laite on tarkoitettu käytettäväksi vain tuotteen pakkauksessa olevan laajentimen ja johtimen kanssa.

### 1.2.6 Muut laitteen kanssa käytettäväksi tarkoitetut laitteet ja tuotteet

FemoSeal™ VCS ei vaadi lisälaitteita toimiakseen tarkoitetulla tavalla.

## 1.3 Riskit ja varoitukset

### 1.3.1 Jäännösriskit ja haittavaikutukset

FemoSeal™ VCS:n käyttöön liittyvistä jäännösriskeistä johtuvat tunnetut tai ennakoitavissa olevat haittavaikutukset, haitat ja komplikaatiot on lueteltu **taulukossa 1.2**. Esiintymistiheys perustuu riskidokumentaation analyysiin ja on laskettu markkinoille saattamisen jälkeisen seurannan tietojen perusteella 1.9.2019–31.8.2024. FemoSeal™ VCS -laitteella ei ole tuntemattomia jäännösriskejä, ja kaikki soveltuvat riskit on käsitelty käyttöohjeissa ja riskienhallintaprosessissa.

**Taulukko 1.2. FemoSeal-laitteen haittatapahtumat/komplikaatiot**

| Haitta                            | Esiintymistiheys (%) | Lieventävät tekijät                                                                                                                                                |
|-----------------------------------|----------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Allerginen reaktio                | 0,0000               | Riskiä mahdollisimman paljon lieventäviä toimenpiteitä ja suunnitelmia ovat tuotesuunnitteluominaisuudet, valmistusohjeet, tuotemerkinnät ja lääkäreiden koulutus. |
| Aneurysma                         | 0,0000               |                                                                                                                                                                    |
| AV-fisteli                        | 0,0001               |                                                                                                                                                                    |
| Verenhukka/verenvuoto             | 0,0280               |                                                                                                                                                                    |
| Kuolema                           | 0,0002               |                                                                                                                                                                    |
| Ekkymoosi                         | 0,0000               |                                                                                                                                                                    |
| Embolia                           | 0,0000               |                                                                                                                                                                    |
| Vierasesinereaktio                | 0,0000               |                                                                                                                                                                    |
| Hematooma                         | 0,0027               |                                                                                                                                                                    |
| Verenvuoto                        | 0,0001               |                                                                                                                                                                    |
| Infektio                          | 0,0002               |                                                                                                                                                                    |
| Tulehdusreaktio                   | 0,0000               |                                                                                                                                                                    |
| Tunnottomuus                      | 0,0000               |                                                                                                                                                                    |
| Kipu                              | 0,0000               |                                                                                                                                                                    |
| Potilaan epämukavuus              | 0,0004               |                                                                                                                                                                    |
| Toimenpiteen viivästyminen        | 0,0065               |                                                                                                                                                                    |
| Valeaneurysma                     | 0,0004               |                                                                                                                                                                    |
| Retroperitoneaalinen verenvuoto   | 0,0002               |                                                                                                                                                                    |
| Sepsis                            | 0,0000               |                                                                                                                                                                    |
| Tromboembolia                     | 0,0000               |                                                                                                                                                                    |
| Tromboosi                         | 0,0001               |                                                                                                                                                                    |
| Suonitukos / alaraajan iskemia    | 0,0002               |                                                                                                                                                                    |
| Verisuonen puhkeama               | 0,0000               |                                                                                                                                                                    |
| Verisuonikudoksen dissektio/haava | 0,0003               |                                                                                                                                                                    |

### 1.3.2 Varoitukset ja varotoimet

#### Varoitukset

1. Ei saa käyttää, jos pakkaus on vaurioitunut tai jos steriili pakkaus ei ole ehjä.
2. Ei saa käyttää viimeisen käyttöpäivämäärän jälkeen – biohajoavat osat eivät välttämättä toimi kunnolla.
3. Ei saa käyttää, jos pakkauksessa olevat osat näyttävät vaurioituneilta tai viallisilta.
4. FemoSeal™ Vascular Closure Systemin käyttö siinä tapauksessa, jos toimenpideholkissa tai ympäröivässä kudoksessa esiintyy bakteerikontaminaatiota, voi aiheuttaa infektion.
5. Jos on syytä epäillä, että valtimon takaseinä on puhjennut tai valtimopunktioita on tehty enemmän kuin yksi, valtimon hemostaasin aikaan saamisessa ei saa luottaa pelkästään FemoSeal™ Vascular Closure Systemiin. Käytä lisäksi manuaalista tai mekaanista painamista.
6. Jos punktiokohta on reisivaltimon haarautumiskohdassa tai distaalisesti siihen nähden, FemoSeal™ Vascular Closure Systemiä ei saa käyttää, koska sisätiiviste voi sijaita väärässä kohdassa. Tämä voi johtaa verenvuotokomplikaatioihin ja/tai veren normaalin virtauksen häiriintymiseen.
7. Jos haava-alueella esiintyy jatkuvaa valtimoverenvuotoa, älä leikkaa monisäikeistä lankaa ennen kuin hemostaasi on saavutettu. Jos hemostaasia ei saada aikaan, kiinnitä monisäikeinen lanka steriilillä haavasidoksella ja paina lisäksi, kunnes hemostaasi saavutetaan. Jatkuvan valtimoverenvuodon yhteydessä voi ilmetä huomattavia verenvuotokomplikaatioita, jotka voivat johtaa potilaan vammautumiseen tai kuolemaan.
8. Älä käytä FemoSeal™ Vascular Closure Systemiä, jos punktiokohta sijaitsee proksimaalisesti nivussiteeseen nähden, sillä se voi aiheuttaa retroperitoneaalisen hematooman.
9. Potilaat, joilla on normaalia suurempi verenvuotoriski, voivat menettää enemmän verta ja tarvita verensiirtoa.
10. Jos sisälevy irtaantuu, se voi aiheuttaa tromboosin ja/tai embolian.

#### Varotoimet

1. FemoSeal™ Vascular Closure Systemin aktivointitoimenpiteen saa suorittaa vain lääkäri, jolla on laitteen käyttöön riittävä koulutus.
2. Suorita osittainen reiden varjoainekuvauksen tai ultraääniohjattu reisipunktio ennen FemoSeal™ Vascular Closure Systemin asettamista.
3. Lopeta toimenpide, jos:

- Yhteisen reisivaltimon luumenin läpimitta < 5 mm.
  - Yhteisen reisivaltimon punktiokohdan läheisyydessä on ahtauma ja/tai merkittävä plakki.
  - Valtimopunktio on reisivaltimon haarautumiskohdassa tai distaalisesti siihen nähden.
  - Yhteisen reisivaltimon punktiokohdan läheisyydessä on anomaalisia haaroja tai vaskulaarisia anomaliaita.
4. Jos potilaalla on hematooma, kartioholkin viemisessä oikein valtimoon on oltava erityisen huolellinen.
  5. Käytä yhden seinämän pistotekniikkaa. Älä puhkaise valtimon takaseinämiä.
  6. Noudata aina steriiliä tekniikkaa käyttäessäsi FemoSeal™ Vascular Closure Systemiä.
  7. FemoSeal™ Vascular Closure System on kertakäyttöinen, eikä sitä saa steriloida tai käyttää uudelleen millään tavalla. FemoSeal™-yksikkö on suunniteltu niin, ettei sitä voi käyttää uudelleen.
  8. Jos sisätiivistein paikalleen asettamisen aikana tuntuu odottamatonta vastusta, keskeytä toimenpide.
  9. Jotta sisätiiviste asettuisi oikein paikalleen, aseta peukalosi niin, että painike pääsee ponnahtamaan vapaasti takaisin.
  10. Varmista, että FemoSeal™-yksikön kartioholkin kärki on ihon pinnan alla ennen ulkoisen lukituslevyn asettamista. Ulkoinen lukituslevy voidaan vahingossa asettaa ihon pinnan yläpuolelle potilailla, joilla reisivaltimo ja ihon pinta ovat lähellä toisiaan.
  11. Oikeaan paikkaan asettaminen voi edellyttää viillon tekemistä ihoon ennen asettamista.
  12. Jos sisätiiviste on sisällä valtimossa, mutta painikkeen painaminen kokonaan alas ja ulkoisen lukituslevyn asettaminen ei ole mahdollista, kirurginen toimenpide voi olla tarpeen FemoSeal™-sulkuelementtien poistamiseksi.
  13. Jos samaan reisivaltimoon on tehtävä punktio uudelleen 18 kuukauden kuluessa, uusi punktio on tehtävä vähintään yhden senttimetrin päähän aiemmasta FemoSeal™ Vascular Closure System -laitteen sisäänvientikohdasta.
  14. Neuvo potilasta noudattamaan lääkärin määräyksiä sulkukohdan tarkastuksesta.
  15. Neuvo potilasta pitämään potilaskorttia mukanaan seuraavien 18 kuukauden ajan.

### **Varotoimet kotiuttamisen yhteydessä**

Ennen kuin harkitset kotiuttamista, arvioi potilas seuraavien kliinisten olosuhteiden mukaisesti:

1. Verenvuoto ja/tai hematooma sulkukohdassa.

2. Kipu kävellessä.
3. Merkkejä infektiosta sulkukohdassa.

### 1.3.3 Käyttöturvallisuutta korjaavat toimenpiteet

Yksi FemoSeal™ VCS -laitteeseen liittyvä käyttöturvallisuutta korjaava toimenpide on tehty 1.9.2019 ja 31.8.2024 välisenä aikana.

Vuonna 2022 Terumo pyysi vapaaehtoisesti palauttamaan FemoSeal™ VCS -laitteita, koska valitusten mukaan Elktonissa valmistetun FemoSeal-laitteen prosessi- ja eränhyväksymistestauksessa oli havaittu puutteita työntövoiman mittaamisessa ja takaisinvetovoimassa. Yhteensä 950 yksikköä palautettiin Etelä-Koreasta.

## 1.4 Kliininen arviointi ja markkinoilletulon jälkeinen kliininen seuranta

**Taulukko 1.3** sisältää luettelon FemoSeal™ VCS -laitteen markkinoille tuontiin liittyvistä keskeisistä tutkimuksista sekä markkinoille saattamisen jälkeisiä tutkimuksia ja markkinoille saattamisen jälkeisiä kliinisiä seurantatoimia. Tutkimuksessa käytetty laiteversio on mainittu alla olevassa taulukossa. FemoSeal™ VCS:n ensimmäinen versio (#11200) oli markkinoilla vuoteen 2006 asti, ja seuraava, tällä hetkellä markkinoilla oleva versio (#C11202), julkaistiin vuonna 2006.

**Taulukko 1.3 Tiivistelmä keskeisistä tutkimuksista**

| Toimintaa koskevat eläinkokeet ennen markkinoille saattamista                                                                                                                                                                                                           | Laitteversio               |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                      |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                      |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                      |
| <b>Ensimmäinen kliininen ihmistutkimus</b>                                                                                                                                                                                                                              |                            |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                      |
| <b>Markkinoille saattamisen jälkeen suoritettut kliiniset tutkimukset</b>                                                                                                                                                                                               |                            |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                                                                              | C11202<br>(nykyinen laite) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                                                                                       | C11202<br>(nykyinen laite) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                                                                                                                                                          | C11202<br>(nykyinen laite) |



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|---------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)          | C11202<br>(nykyinen laite) |
| <b>Suunnitellut / meneillään olevat markkinoille saattamisen jälkeiset kliiniset tutkimukset</b>                                |                            |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                      | C11202<br>(nykyinen laite) |
| <b>Kliiniset seurantatoimet markkinoille saattamisen jälkeen</b>                                                                |                            |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(nykyinen laite) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(nykyinen laite) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(nykyinen laite) |

#### 1.4.1 Tiivistelmä markkinoille saattamista edeltävistä tutkimuksista (eläinkokeista ja kliinisistä tutkimuksista)

Alla olevassa **taulukossa 1.4** kuvataan kaikki markkinoille saattamista edeltävät tutkimukset, sekä eläinkokeet että kliiniset tutkimukset.

**Taulukko 1.4 Tiivistelmä markkinoille saattamista edeltävistä tutkimuksista**

| Toimintaa koskevat eläinkokeet ennen markkinoille saattamista                                                                                                                                                                                                           |                                                                       |                                   |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------|-----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Tutkimuksen nimi                                                                                                                                                                                                                                                        | Vuosi/Koordinoiva tutkija                                             | Tutkimuksen tyyppi                | Tavoitteet                                                                                                                                                                                                                                                 | Välitavoitteet                                                                                                                                                                                                                                                                                                   | Mahdolliset hyväksymiskriteerit                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 2000<br>Radi Medical System AB<br><br>Suorittaja<br>Biomatech, Ranska | Eläintutkimus, kokeileva tutkimus | Tutkimuksen tavoitteena oli arvioida biologisesti hajoavan, verisuoniston hemostaasin aikaansaamiseen tarkoitetun implantin bioyhteensopivuutta ja biotoiminnallisuutta. Raportissa mainitaan varaeläimet tutkimuksessa numero 862 (asiakirja nro 1051-01) | N = 3 aikuinen naaraslammas, 1 eläin / aikapiste<br><br>Histopatologisen analyysin, makroskooppisen luokituksen ja hienorakenneanalyysin seuranta<br><br>• 12 kuukautta<br>• 15 kuukautta<br>• 18 kuukautta<br><br>Väridoppler-ultraääniseuranta – 30 päivää kaulavaltimon ja reisivaltimon sisäänvientikohdissa | Valtimoiden avoimuus<br>• Verenvirtauksen arviointi aktivoinnin jälkeen – verenvirtauksen väheneminen 2/3 tapauksista liittyen toimenpiteen yhteydessä todettuun tilapäiseen valtimospasmiin, kumpikin esiintyi vasemmanpuoleisessa yhteisessä kaulavaltimossa<br>• Väridoppler-ultraääniarviointi (4 viikkoa) - 3/3 (100 %) ilman merkittävää verenvirtauksen vähenemistä 30 päivää implantoinnin jälkeen<br><br>Makroskooppiset havainnot<br>• 12 kuukautta – avoimuus vahvistettu makroskooppisesti toteamalla, ettei |

|  |  |  |  |  | <p>anatomisesti näkyvää tukosta ole; ei makroskooppisia paikallisia intoleranssileesioita (verenvuoto, nekroosi tai neovaskulaarisuus); sisälevyn kapseloituminen ilmeisesti pantu merkille</p> <ul style="list-style-type: none"> <li>15 kuukautta – makroskooppisessa tarkastelussa ei havaittu merkkejä tulehduksesta; sisätiivistein tai ulkoisen levyn jäämiä ei havaittu; ulkoisen levyn alueella havaittu kapselointikudos näytti samalta kuin 12 kuukauden kohdalla</li> <li>18 kuukautta – makroskooppisessa tarkastelussa ei havaittu merkkejä paikallisesta sietokyvyttömyydestä, ulkoisen levyn hajoaminen täydellinen (3/3 tapausta), sisälevyn hajoaminen täydellinen; 1/3 (vasen yhteinen kaulavaltimo) – implanttikohdassa havaittu valtimoseinämän painuma (voi liittyä laitteen aktivointiin)</li> </ul> <p>Johtopäätökset</p> <ul style="list-style-type: none"> <li>Makroskooppisesti tarkasteltuna 12, 15 ja 18 kuukautta implantoinnin jälkeen ei havaittu nekroottisia, degeneratiivisia tai tromboottisia merkkejä.</li> <li>Sisälevyn ja ulkoisen levyn hajoamisprosessi näytti etenevän 12 ja 18 kuukauden tarkasteluajankohtien välillä ja näytti täydelliseltä 18 kuukauden kohdalla. Implantoitua aluetta peittää vaalea kudos.</li> <li>Histologisesti tarkasteltuna polymeerimateriaalia ei ollut 18 kuukauden kuluttua enää näkyvissä, mutta kohdassa oli endoluminaalista sidekudosta. Nekroottisia, degeneratiivisia tai tromboottisia leesioita ei havaittu.</li> </ul> |
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|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|-----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 2002 Radi Medical System AB<br><br>Suorittaja Biomatech, Ranska | Eläintutkimus, kokeileva tutkimus | Tutkimuksen tavoitteena oli arvioida biologisesti hajoavan, verisuoniston hemostaasin aikaansaamiseen tarkoitetun implantin bioyhteensopivuutta. | Seuranta (implantaation jälkeen) <ul style="list-style-type: none"> <li>• 12 viikkoa</li> <li>• 24 viikkoa</li> <li>• 36 viikkoa</li> </ul> N = 12 lammasta, 3 eläintä aikapistettä kohti, 3 varaeläintä uhrattu 12, 15 ja 18 kuukauden kohdalla<br><br>Implantointikohdat – oikea ja vasen reisivaltimo, oikea ja vasen yhteinen kaulavaltimo<br><br>Väridoppler-ultraäänianalyysi | <u>Kaulavaltimoiden ja reisivaltimoiden avoimuus 4 viikon jälkeen</u> <ul style="list-style-type: none"> <li>• Huomattava verenvirtauksen väheneminen 0/12 (0 %)</li> </ul> <u>Ei merkittävää verenvirtauksen vähenemistä</u> <ul style="list-style-type: none"> <li>• Vaikea verenvirtauksen heikentyminen, joka liittyy laitteen sisäänvientiin 0/12 (0 %)</li> <li>• Verenvirtauksen väheneminen vasemmassa yhteisessä kaulavaltimossa 2/12 (16,6 %) tilapäisen valtimospasmin vuoksi (mikä johtui leikkauksesta, ei laitteesta)</li> </ul> <u>Verenvirtauksen heikentyminen seurannan mukaan</u> 12 viikkoa – 0/12 (0 %)<br>24 viikkoa – 0/12 (0 %)<br>36 viikkoa – 0/12 (0 %)<br><br>Verenpaineen mittausta (3 lammasta – 36 vko) <ul style="list-style-type: none"> <li>• Merkittävää verenvirtauksen vähenemistä ei havaittu</li> </ul> Makroskooppiset tiedot integroitumisesta ja hajoamisesta (aste 0–4)<br><br><u>Kaulavaltimot</u><br><u>Sisäpuoli</u> - kapseloituminen<br>12 viikkoa 1,3<br>24 viikkoa 0,8<br>36 viikkoa 0,7<br>- materiaalin hajoaminen<br>12 viikkoa 2,2<br>24 viikkoa 2,3<br>36 viikkoa 0,7<br><u>Ulkopuoli</u> - kapseloituminen<br>12 viikkoa 2,0<br>24 viikkoa 1,0 |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|-----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | 36 viikkoa 0,8<br>- materiaalin hajoaminen<br>12 viikkoa 2,0<br>24 viikkoa 2,7<br>36 viikkoa 3,2<br><br><u>Reisivaltimot</u><br><u>Ulkopuoli</u><br>- kapseloituminen<br>12 viikkoa 1,0<br>24 viikkoa 2,7<br>36 viikkoa 1,0<br>- materiaalin hajoaminen<br>12 viikkoa 2,0<br>24 viikkoa 2,4<br>36 viikkoa 3,0<br><br><u>Sisäpuoli</u><br>- kapseloituminen<br>12 viikkoa 2,0<br>24 viikkoa 1,2<br>36 viikkoa 1,0<br>- materiaalin hajoaminen<br>12 viikkoa 1,0<br>24 viikkoa 2,2<br>36 viikkoa 3,0<br><br><u>Histologiset tiedot</u><br><u>integroitumisesta, hajoamisesta</u><br><u>ja tulehdusparametreista</u><br><u>(oleellisten arvojen keskiarvo,</u><br><u>indeksi 0–4) n=6</u><br><br><u>Kaulavaltimot</u><br>Ulkoinen fibroosi<br>12 viikkoa – 2,3<br>24 viikkoa – 2,3<br>36 viikkoa – 1,8<br>Sisäinen arpikudos<br>12 viikkoa – 3,0<br>24 viikkoa – 2,7<br>36 viikkoa – 3,3<br>Materiaalin hajoaminen<br>12 viikkoa – 1,7<br>24 viikkoa – 3,0<br>36 viikkoa – 3 +<br>Tulehdusparametrit<br>(makrofagit)<br>12 viikkoa – 3,0<br>24 viikkoa – 1,7<br>36 viikkoa – 1,7 |
|--|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | <u>Reisivaltimot</u><br>Ulkoinen fibroosi<br>12 viikkoa – 1,3<br>24 viikkoa – 1,5<br>36 viikkoa – 1,7<br>Sisäinen arpikudos<br>12 viikkoa – 3,7<br>24 viikkoa – 3,3<br>36 viikkoa – 3,8<br>Materiaalin hajoaminen<br>12 viikkoa – 2,0<br>24 viikkoa – 3,0<br>36 viikkoa – 3+<br>Tulehdusparametrit<br>(makrofagit)<br>12 viikkoa – 3,5<br>24 viikkoa – 1,8<br>36 viikkoa – 1,8<br><br><u>Histomorfologisen avoimuuden arvot</u><br>Kaulavaltimot<br>12 viikkoa 74,0 %<br>24 viikkoa 81,9 %<br>36 viikkoa -89,43 %<br>Reisivaltimot<br>12 viikkoa – 42,2 %<br>24 viikkoa – 73,21 %<br>36 viikkoa – 78,71 %<br><br><u>Verisuonten avoimuus UÄ (keskiarvo-%)</u><br>Kaulavaltimo<br>12 viikkoa 94,6 %<br>24 viikkoa – 96,7 %<br>36 viikkoa – 94,7 %<br>Reisivaltimo<br>12 viikkoa – 66,9 %<br>24 viikkoa – 63,6 %<br>36 viikkoa – 75,1 %<br><br>Johtopäätökset <ul style="list-style-type: none"> <li>• Merkittävää paikallista merkkiä sietokyvyttömyydestä (ei näkyviä tulehduksellisia, nekroottisia tai degeneratiivisia leesioita) ei havaittu 12, 24 tai 36 viikon kohdalla</li> <li>• Isännän kudoksessa ei havaittu merkittäviä</li> </ul> |
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|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------|----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France). | 2002<br><br>Radi Medical System AB<br><br>Suorittaja Biomatech, Ranska | Eläinkoe | Tutkimuksen tavoitteena oli arvioida biologisesti hajoavan, verisuoniston hemostaasin aikaansaamiseen tarkoitettujen implanttien biokyhteensopivuutta ja biotoiminnallisuutta. Testattu laite on tarkoitettu viettäväksi valtimon punktiokohtaan hemostaasin saavuttamiseksi. Toinen levy vietiin punktioreiästä sisään valtimoon ja toisella kiristettiin sisälle viety levy valtimon ulkopuolelta käsin. Kumpikin levy vietiin sisään sisäänviejän avulla. Levyjen on tarkoitus estää verenvuotoa, parantua suonien seinämää vasten ja lopulta hajota ja resorboitua. Tutkimus suunniteltiin keräämään ja analysoimaan tietoja lampailla ja sioille tehdyn toiminnallisen implantoinnin jälkeen, jotta voidaan arvioida implantin kapasiteettia fysiologisen toiminnan ylläpitämiseksi verenkiertojärjestelmässä, määrittää isännän ja laitteen vastetta (fyysinen keho, kudoksenselotuminen uhrauksen ajankohtana) sekä arvioida implantin hajoamista. | Implantaatiojakso / seuranta-aika on 5 viikkoa kaikille eläimille<br><br>4 lammasta, 1 sika<br><br>14 sulkuelementtiä<br><br>8 sulkuelementtiä implantoitu 2 lampaalle,<br><br>2 sulkuelementtiä implantoitu 1 sialle<br><br>Kun kaksi sulkuelementtiä implantoitiin samaan reisivaltimoon, ne implantoitiin > 30 mm:n etäisyydelle toisistaan | Kaikki haittavaikutuksista kertovat kriteerit (tulehdus, nekroosi, verenvuoto tai muu leesio) ja mahdollisen ohuen pseudointimaalikerroksen muodostuminen kirjattiin. Erityistä huomiota kiinnitettiin laitteen integroitumiseen alkuvaiheessa, jossa painotettiin erityisesti sisälevyn kapseloitumista.<br><br>Makroskooppisesti ei havaittu merkittäviä merkkejä paikallisesta sietokyvyttömyydestä tai suonensisäisen hyttymän muodostumisesta. Makroskooppisessa tarkastelussa ei havaittu eroa lampaiden ja sikojen välillä reisivaltimoiden sulkuelementtien implantoinnin jälkeen. Makroskooppisesti ei havaittu merkittäviä merkkejä paikallisesta sietokyvyttömyydestä tai suonensisäisen hyttymän muodostumisesta. Makroskooppisessa tarkastelussa ei havaittu eroa lampaiden ja sikojen välillä reisivaltimoiden sulkuelementtien implantoinnin jälkeen.<br><br>Lampaalla asetuskohtaan histopatologisessa analyysissä ei havaittu paikallisia haittavaikutuksia. Sisälevyssä ja ulkoisessa |

|                                                                                                                                          |                                  |                                        |                                                                                                                                                             |                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
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|                                                                                                                                          |                                  |                                        |                                                                                                                                                             |                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|                                                                                                                                          |                                  |                                        |                                                                                                                                                             |                                                                                           | <p>levyssä oli hajoamisen merkkejä, ja joissakin tapauksissa ne olivat murtuneet pienemmiksi osiksi. Sisälevyt olivat täysin integroituneet neointimaaliseen kudokseen. Sialla sisälevyn ja ulkoisen levyn ympärillä todettiin histopatologisessa analyysissä hieman enemmän merkkejä tulehduksesta. Molemmilla eläimillä monisäikeisessä langassa oli hieman enemmän merkkejä tulehduksesta kuin levymateriaalissa, mikä on normaalia punotun ommelaineen suuremman pinta-alan vuoksi.</p> <p>Suonen avoimuus mitattiin 5 viikon kuluttua kolmella eri menetelmällä, histomorfometrisesti, histomorfometrisesti yhdistettynä suonen läpimitan mittaukseen työntömitalla ja väridoppler-ultraäänitutkimuksella. Suonen keskimääräinen avoimuus lampailla oli 60–80 % menetelmästä riippuen (12 havaintoa). Sialla suonen keskimääräinen avoimuus oli 40–80 % (2 havaintoa).</p> |
| <b>Ensimmäinen kliininen ihmistutkimus</b>                                                                                               |                                  |                                        |                                                                                                                                                             |                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| <b>Tutkimuksen nimi</b>                                                                                                                  | <b>Vuosi/Koordinoiva tutkija</b> | <b>Tutkimuksen tyyppi</b>              | <b>Tavoitteet</b>                                                                                                                                           | <b>Välitavoitteet</b>                                                                     | <b>Mahdolliset hyväksymiskriteerit</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Intervention | 2004 Radi Medical Systems AB     | Avoin yksihaarainen monikeskustutkimus | Tutkimuksen tavoitteena oli määrittää FemoSeal Vascular Closure Systemin (FemoSeal System) turvallisuus, suorituskyky ja tehokkuus yleisesti ja erityisesti | 2-osainen tutkimus<br><br>Yhteensä n = 80<br>Osa 1 n = 20<br>Osa 2 n = 60<br>Indikaatiot: | Tulokset<br>- <u>hemostaasi saavutettu FS:llä ilman kompressiota</u><br>- Osa 1 20/20 (100 %)<br>- Osa 2 58/60 (97 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |

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| nal Cardiology<br>Procedures (EU-SE-<br>001); 2004, Radi<br>Medical Systems AB. |  |  | sulkuelementtien osalta<br>potilailla, joille tehdään<br>diagnostisia tai<br>interventiokardiologisia<br>toimenpiteitä reisivaltimon<br>kautta. | Osa 1 – diagnostinen<br>sydänkatetrointi käyttämällä<br>reisivaltimoa<br>sisäänvientikohtana<br><br>Osa 2 – potilaat, joille<br>suoritetaan diagnostisia ja<br>interventioon perustuvia<br>sydäntoimenpiteitä käyttämällä<br>reisivaltimoa<br>sisäänvientikohtana<br><br>30 päivän seuranta | Hemostaasiajan mediaani<br>toimenpiteen yhteydessä<br>(osa 2) - 1,0 minuuttia<br>(alue: välittömästi –<br>8 minuuttia)<br><br><u>Liikkeellelähtöaika</u><br><u>(minuutteina)</u><br>Osa 1 -<br>Mediaani: 33,0<br>keskiarvo: 67,8<br>Osa 2 –<br>Mediaani: 45<br>keskiarvo: 87,5<br><br><u>Merkittävien</u><br><u>verisuonikomplikaatioiden</u><br><u>esiintyminen – 30 päivän</u><br><u>seuranta</u><br>Osa 1<br>- Ei<br>verisuonikomplikaatioita<br>20/20 (100 %)<br>Osa 2<br>Pseudoaneurysma – 1/59<br>(1,69 %)<br><br><u>Hoidon epäonnistuminen</u><br>Osa 1 – 0/20 (0 %)<br>Osa 2 – 3/60 (5 %)<br>• 2 johtuen siitä, että<br>hemostaasia ei<br>saavuttu ilman<br>kompressiota<br>• 1 vakavasta<br>verisuonikomplikaatioi<br>sta johtuen,<br>pseudoaneurysma<br><br><u>Jatkuva tihkuminen</u><br>Osa 1 – 0/20 (0 %)<br>Osa 2 – 8/60 (13 %)<br><br><u>Hematooma</u><br>Osa 1 – 0/20 (0 %)<br>Osa 2 – 6/60 (10 %) |



Osana FemoSeal™ VCS:n markkinoille saattamista edeltävää kehityssuunnitelmaa tehtiin kolme toimintaa testaavaa eläinkoetta. Vuonna 2000, ennen kliinisten tutkimusten aloittamista tehtiin eläintutkimus, jossa arvioitiin FemoSeal™ VCS:n biotoiminnallisuutta. Tässä tutkimuksessa arvioitiin sulkuelementtien kykyä ylläpitää fysiologista toimintakykyä ja arvioida niiden hajoamista. 18 kuukauden kuluttua sisä- ja ulkolevyymateriaali eivät enää näkyneet, vaan ne olivat korvautuneet endoluminaalisella sidekudoksella. Yhteenvetona voidaan todeta, että tutkimuksessa vahvistettiin FemoSeal™ VCS -sulkuelementin kyky pitää yllä fysiologista toimintaa, kun sitä käytettiin verenkiertojärjestelmässä.

Vuonna 2002 tehtiin eläintutkimus, jossa arvioitiin biohajoavan FemoSeal™ VCS -implantin bioyhenteensopivuutta ja biotoiminnallisuutta. Implantti on suunniteltu hemostaasin aikaansaamiseen verisuonijärjestelmässä. Yhteenvetona voidaan todeta, että implantti oli hajonnut lähes kokonaan 36 viikon kuluttua, eikä merkittäviä haitallisia kudosreaktioita ollut.

Eräässä toisessa eläintutkimuksessa vuonna 2002 arvioitiin biohajoavan FemoSeal™ VCS -implantin bioyhenteensopivuutta ja biotoiminnallisuutta. Implantti on suunniteltu hemostaasin aikaansaamiseen verisuonijärjestelmässä. 5 viikon kuluttua levyn kapseloituminen oli täydellinen ja sisä- ja ulkolevyissä havaittiin hajoamisen merkkejä. Yhteenvetona voidaan todeta, että tutkimuksessa vahvistettiin implantin kyky ylläpitää fysiologista toimintakykyä verenkiertojärjestelmässä käytettäessä.

Osana FemoSeal™ VCS:n kliinistä kehityssuunnitelmaa Radi Medical System AB suoritti markkinoille saattamista edeltävän kliinisen tutkimuksen. Tätä kliinistä tutkimusta ei ole julkaistu tai saatavilla verkossa. Laitemallia #11200 koskeva tutkimus toteutettiin vuosina 2002–2004 eurooppalaisen standardin EN 540 (Ihmisille terveydenhuollon laitteilla ja tarvikkeilla suoritettavat kliiniset tutkimukset) mukaisesti ja ICH:n kliinisiä tutkimuksia koskevien yleisten näkökohtien ja hyvien kliinisten käytäntöjen ohjeiden mukaisesti. Tämän tutkimuksen tiedot on dokumentoitu raportissa EU-SE-001. Kliininen tutkimus dokumentoitiin Radi Medical Systems AB:n loppuraportissa “Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures”. Kliininen tutkimus suoritettiin FemoSeal™-laitteen ensimmäisellä mallilla #11200, ja siinä keskityttiin implantoitavien sulkukomponenttien turvallisuuteen ja tehoon. Ainoa ero ensimmäisen mallin #11200 ja nykyisen mallin C11202 välillä on F-koko, ensimmäisessä 6F ja nykyisessä 7F, sekä parannettu toimitusjärjestelmä. Implantoitavien sulkuelementtien, sisätiivisteiden ja ulkoisen lukituslevyn kliiniset hyödyt, käyttötarkoitus, käyttöperiaatteet ja raakamateriaalit pysyvät ennallaan.

Laite on tarkoitettu käytettäväksi potilailla, joille tehdään diagnostisia tai interventioon perustuvia sydäntoimenpiteitä reisivaltimon kautta. Tämän tutkimuksen tavoitteena oli määrittää FemoSeal™ VCS -laitteen turvallisuus, suorituskkyky ja teho. Kyseessä oli prospektiivinen, yhden tutkimushaaran avoin monikeskustutkimus, johon kuului 30 päivän seuranta.

Suorituskykyyn liittyvä ensisijainen päätetapahtuma oli hemostaasin aikaan saamiseen kuluva aika, jossa hemostaasi määriteltiin riskialttiin verenvuodon puuttumiseksi. Turvallisuuteen liittyvä ensisijainen päätetapahtuma oli vakavien verisuonikomplikaatioiden ilmaantuvuus 30 vuorokauden kuluessa. Toissijaisia päätetapahtumia olivat liikkeellelähtöaika, epäonnistuneiden hoitojen osuus, haittatapahtumien ilmaantuvuus ja laitteen suorituskykyominaisuudet toimituksen ja aktivoinnin aikana.

Tutkimukseen osallistuvat potilaat olivat aikuisia, jotka pystyivät antamaan tietoon perustuvan suostumuksen ja joilla oli vähintään yksi tuntuva jalan valtimon syke. Potilas suljettiin pois tutkimuksesta, jos tällä oli jokin seuraavista tiloista:

- Aiempi ääreisverisuonisairaus
- Autoimmuunisairaus
- Tunnettu verenvuotohäiriö tai vaikea-asteinen anemia
- INR >1,5
- Sydäninfarkti 72 tunnin kuluessa
- Hallitsematon hypertensio hoidosta huolimatta
- Seldinger-tekniikalla avaamisen estävä liikalihavuus
- Verisuonisiirre tai stentti arteriotomiakohdassa
- Edellinen ipsilateraalinen punktio 3 kuukauden sisällä
- Odotettavissa oleva elinaika < 6 kuukautta

Lisäksi potilaita tutkittiin toimenpiteen aikana, ja heidät suljettiin pois tutkimuksesta, jos havaittiin mitään seuraavista:

- Yhteisen reisivaltimon lumenin läpimitta <5 mm
- Valtimohaaroja enintään 2 cm:n päässä punktiokohdasta
- Merkittävä ahtauma enintään 3 cm:n päässä punktiokohdasta
- Käytössä olevan ensisijaisen sisäänviejäholkin koko > 6 F
- Punktiokohta reisivaltimon haarautumiskohdassa tai distaalisesti siihen nähden
- Useita reisivaltimon punktiokohtia
- Tiedossa oleva tai epäilty reisivaltimon takaseinän puhkeama
- Suuri hematooma (2:6 cm) toimenpiteen päätyttyä
- Ensisijaisen holkin sisäänvienti toimenpidettä varten hankalaa kiertyneen kudoksen tai suonen vuoksi

Yhteen tutkimussuunnitelmaan perustuva tutkimus toteutettiin kahdessa osassa: Osaan 1 otettiin 20 potilasta, minkä jälkeen tehtiin turvallisuusanalyysi, jonka jälkeen otettiin 60 potilasta lisää osan 2 aikana.

Osassa 1 tutkimukseen otettujen potilaiden keski-ikä oli 65,9 vuotta, 70,0 % potilaista oli miehiä ja 95 % potilaista käytti samanaikaisesti lääkkeitä. Tutkimuksen osassa 2 keski-ikä oli 63,8 vuotta, 78 % oli miehiä ja 100 % käytti samanaikaisesti lääkkeitä.

Tutkimukseen kelpuutettiin potilaita, joille tehtiin diagnostisia (osa 1 ja osa 2) tai interventioon perustuvia (osa 2) sydämen katetrointitoimenpiteitä. Toimenpiteissä noudatettiin jokaisen mukana olevan sairaalan hoitokäytäntöjä, minkä jälkeen käytettiin FemoSeal™ VCS -laitetta. Potilastietoja kerättiin tutkimuksen alussa, toimenpiteen aikana sekä yhden ja 30 päivän kuluttua toimenpiteestä. Tulokset esitetään tiivistelmänä **taulukossa 1.5**, ja ne osoittavat, että FemoSeal™ VCS -laitteen käyttö on turvallista ja tehokasta tässä potilasryhmässä.

**Taulukko 1.5 Markkinoille saattamista edeltävässä tutkimuksessa raportoidut kliiniset tulokset**

|                                                                                                                      | Osa 1          | Osa 2                       |
|----------------------------------------------------------------------------------------------------------------------|----------------|-----------------------------|
| Potilaiden määrä                                                                                                     | 20             | 60                          |
| Hemostaasiajan keskiarvo                                                                                             | 1,2 minuuttia  | 1,6 minuuttia <sup>a</sup>  |
| Keskimääräinen liikkeellelähtöaika                                                                                   | 72,2 minuuttia | 87,5 minuuttia <sup>b</sup> |
| Merkittävien verisuonikomplikaatioiden esiintyminen <sup>c</sup>                                                     | 0 (0 %)        | 1 (2 %)                     |
| Haattatapahtumapotilaiden määrä                                                                                      | 5 (25 %)       | 19 (32 %)                   |
| Hoidon epäonnistuminen (määritelmänä merkittävät verisuonikomplikaatiot, manuaalisen kompression tarve tai molemmat) | 0 (0 %)        | 3 (5 %)                     |
| Laitteen toimintahäiriöt                                                                                             | 0 (0 %)        | 6 (10 %)                    |

<sup>a</sup> Perustuu kokonaisotokseen 58, koska 2 potilaalle ei saatu aikaan hemostaasia toimenpiteen aikana aiempien ipsilateraalisten pistosten vuoksi. Näillä potilailla hemostaasi saavutettiin 7 minuutin ja 37 minuutin kuluttua.

<sup>b</sup> Perustuu kokonaisotokseen 59: 1 potilas ei ollut mukana, koska hänet asetettiin hengityslaitteeseen keuhkoedeeman vuoksi eikä hän pystynyt liikkumaan yli viikkoon.

<sup>c</sup> Määritellään verisuonikomplikaatioksi, joka edellyttää verensiirtoa tai kirurgista korjausta, tai paikalliseksi infektioksi, joka edellyttää antibioottien antamista, sairaalahoitoa tai sairaalahoidon pidentämistä tai haavan puhdistamista.

Tutkimuksen osassa 1 ei todettu merkittäviä verisuonikomplikaatioita. Tutkimuksen osassa 2 raportoitiin yksi merkittävä verisuonikomplikaatio: pseudoaneurysma, joka raportoitiin yhden päivän kuluessa toimenpiteestä. Tapahtuma edellytti ultraääniohjattua kompressiota ja trombiinin injektointia valeaneurysmaan, ja se pidensi potilaan sairaalassaoloa.

Tutkimuksen osassa 1 ilmoitetuista viidestä haattatapahtumasta yksi oli mahdollisesti laitteeseen liittyvä haattatapahtuma: ei-vakava tapahtuma, jossa riskiverenvuoto ilmeni yhden päivän kuluttua toimenpiteestä. Tutkimuksen osassa 2 ilmoitetuista 19 haattatapahtumasta kolmessa tapahtumassa oli kyse laitteeseen liittyvästä, ei-vakavasta haattatapahtumasta eli hematoomasta, ja kuudessa tapahtumassa oli kyse laitteeseen mahdollisesti liittyvästä, ei-vakavasta tapahtumasta, joista kolme oli pitkittynyttä tihkumista, kaksi hematoomaa ja yksi jalkakipu liikunnan jälkeen.

Osassa 2 hoidon katsottiin epäonnistuneen kolmen potilaan kohdalla: kahdessa tapauksessa hemostaasia ei saatu aikaan ilman kompressiota, ja yksi johtui vakavasta verisuonikomplikaatiosta (pseudoaneurysma). Tutkimuksen osassa 1 ei esiintynyt hoidon epäonnistumista.

Kuudesta laitteen toimintahäiriöstä tutkimuksen osassa 2 kolme ei vaikuttanut toimenpiteeseen, yksi johtui käyttäjän virheestä, yksi vuotavasta sisäänviejästä ja yksi rikkoutuneesta kuituliitoksesta. Kaksi viimeistä käsiteltiin mallipäivityksillä, jotka otettiin käyttöön mallissa C11202.

Markkinoille saattamista edeltävän kliinisen tutkimuksen osa 2 ei raportoinut 6 kuukauden seurantatuloksista johtuen potilaan ohjeiden noudattamatta jättämisestä. Markkinoille saattamista edeltävän kliinisen tutkimuksen (EU-SE-001) 30 päivän tulokset osoittavat, että FemoSeal™ VCS on turvallinen ja tehokas. Seuranta-aika on kliinisen kirjallisuuden mukainen.

#### 1.4.2 Tiivistelmä markkinoille saattamisen jälkeen toteutetuista kliinisistä tutkimuksista

Alla olevassa **taulukossa 1.6** on kuvattu neljä markkinoille saattamisen jälkeen suoritettua kliinistä tutkimusta. Näitä kliinisiä tutkimuksia ei ole julkaistu tai saatavilla verkossa.

**Taulukko 1.6 Markkinoille saattamisen jälkeen suoritettut kliiniset tutkimukset**

| Markkinoille saattamisen jälkeen suoritettut kliiniset tutkimukset                          |                           |                                                                                            |                                                                                                                                                                             |                                                                                                                                                                                    |                                                                                                                                                                      |
|---------------------------------------------------------------------------------------------|---------------------------|--------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Tutkimuksen nimi                                                                            | Vuosi/Koordinoiva tutkija | Tutkimuksen tyyppi                                                                         | Tavoitteet                                                                                                                                                                  | Välitavoitteet                                                                                                                                                                     | Mahdolliset hyväksymiskriteerit                                                                                                                                      |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI              | Markkinoille saattamisen jälkeinen tutkimus, uuden pakkauksen hyväksyttävyyden käyttäjille | Markkinoille saattamisen jälkeinen tutkimus koskien FemoSeal® Vascular Closure Systemin #11202 uutta mallia, jossa on muutettu toimitusjärjestelmää verrattuna ensimmäiseen | 100 potilasta <ul style="list-style-type: none"> <li>63 miestä / 37 naista</li> <li>Naisten keski-ikä 68 vuotta, miesten 65 vuotta</li> </ul> 2 ruotsalaista sairaalaa, 6 lääkäriä | Tulokset <ol style="list-style-type: none"> <li>Käyttöohjeissa olevat kuvat/ohjeet ovat informatiivisia ja riittäviä</li> <li>Välitön hemostaasi (91/100)</li> </ol> |

|                                                                                   |                                                            |                                                         |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
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|                                                                                   |                                                            |                                                         | <p>malliin #11200, toimivuuden dokumentoimiseksi.</p> <p>Tutkimuksen tavoitteena oli saada palautetta päivitetystä käyttöohjeista sekä lääkäreiden ja hoitajien koulutusprojektista, vahvistaa riskianalyyseissa tehtyjä arviointeja ja saada tietoja tuotteen laadun paranemisesta.</p> | <p>112 laitetta</p> <p>Potilastietolomakkeille tallennetut tiedot (CRF)</p> <p>Suunniteltu tarkkailuaika – 30 minuuttia aktivoinnista</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008) | Tri Nicolas Moes<br>Innsbruck Medical University, Itävalta | Markkinoille saattamisen jälkeinen vahvistava arviointi | <p>Tutkimuksen tavoitteena oli arvioida FemoSeal®-laitteen turvallisuutta ja suorituskykyä normaalien kliinisten rutiinien yhteydessä potilailla, joille tehdään diagnostinen sydämen katetrointi tai perkutaaninen sydämen interventiotoinenpide 7F-holkilla.</p>                       | <p>50 peräkkäistä potilasta</p> <p>Indikaatio – diagnostinen tai invasiivisen sydämen katetrointi yhteisen reisivaltimon kautta</p> <table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.6±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.6±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | <p>Ensisijaiset päätetapahtumat</p> <ul style="list-style-type: none"><li>Tehoa koskeva ensisijainen päätetapahtuma – Hemostaasiaika (TTH) joko tihkuen tai ilman tihkumista, mutta ilman lisäkompressiota, manuaalista tai mekaanista.</li><li>Turvallisuutta koskeva päätetapahtuma – haittavaikutusten esiintyvyys – pienet ja vakavat verisuonikomplikaatiot ja kaikki muut haittavaikutukset – vakavat ja ei-vakavat tutkimuksen aikana (eli potilaan kotiuttamiseen asti).</li></ul> <p>Tulokset</p> <ul style="list-style-type: none"><li>Hemostaasiajan keskiarvo</li><li>Diagnostinen – 56,6 ± 29 sekuntia</li><li>Interventionaalinen 59,9 ± 16,2 sekuntia</li><li>Kaikki potilaat 57,8 ± 26,3</li><li>Kaikki potilaat pystyivät liikkumaan neljän tunnin vuodelevon jälkeen ongelmitta.</li></ul> <p>Turvallisuutta koskevat tulokset</p> <ul style="list-style-type: none"><li>49/50 (98 %) ei kokenut verisuonikomplikaatioita sairaalasta kotiuttamiseen mennessä</li><li>Keskimääräinen kotiutusaika 2,6 päivää</li></ul> |
| n                                                                                 | 50                                                         |                                                         |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| men                                                                               | 35 (70%)                                                   |                                                         |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| women                                                                             | 15 (30%)                                                   |                                                         |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| PCI cases                                                                         | 15                                                         |                                                         |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| age (yrs)                                                                         | 62.6±11.1                                                  |                                                         |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| body mass index (kg/m²)                                                           | 25.4±6.7                                                   |                                                         |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| systolic BP (mmHg)                                                                | 131.2±20.9                                                 |                                                         |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| diastolic BP (mmHg)                                                               | 77.9±10.6                                                  |                                                         |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| diabetes mellitus                                                                 | 9 (18%)                                                    |                                                         |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| arterial hypertension                                                             | 34 (68%)                                                   |                                                         |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| previous coronary intervention                                                    | 13 (26%)                                                   |                                                         |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| preprocedure aspirin                                                              | 50 (100%)                                                  |                                                         |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| preprocedure clopidogrel                                                          | 50 (100%)                                                  |                                                         |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Procedural unfractionated heparin                                                 | 15 (30%)                                                   |                                                         |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Procedural abciximab                                                              | 2 (4%)                                                     |                                                         |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |

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|                                                                                                                                 |                                   |                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | <ul style="list-style-type: none"> <li>1/50 (2 %) vähäistä verenvuotoa seuraavana päivänä, kun angiografiapäivänä on liikuttu ongelmitta</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | 2009 RADI                         | Markkinoille saattamisen jälkeinen tutkimus                                         | Tutkimuksesta tulisi käydä ilmi, onko asiakkailla/käyttäjillä havaittu ongelmia uuden pakkauksen kanssa, erityisesti Tyvek/PET-PE-pussin ei-steriilin ulkopinnan kanssa.<br><br>Tutkimuksessa pyritään saamaan myös tietoja siitä, havaitseeko hoitava lääkäri mitään eroa laitteen käyttö-/aktivointivaiheissa verrattuna aiemmin käytettyihin laitteisiin.<br><br>Tutkimuksessa pitäisi myös saada palautetta mahdollisista muista tuotelaadun parantamistarpeista. | 25 laitetta<br>4 ruotsalaista sairaalaa<br><br>16/25 (64 %) potilaista oli PCI-potilaita, joilla oli voimakas antikoagulaatiolääkitys                                                                                                                                                                                                                                                                                                                                                                  | Tulokset<br>1. Pakkaukseen liittyvät ongelmat – 21/25 (84 %) käyttökertoista onnistui; 4/25 (16 %) ei onnistunut (1 – uuden sisäänviejän testaaminen, 1 sisälevy mennyt arteriotomian läpi poisvetovaiheessa, painike tullut esiin ja ulkolevy asettunut kudoksanavaan viillon kohdalla, 2 välitöntä hemostaasia ei saavutettu huolimatta siitä, ettei aktivoimisessa ollut ongelmia.)<br>2. Välitön hemostaasi 19/25 (76 %) potilaalla<br>3. Verenvuoto 11/25 (44 %) - 9/25 (36 %), tiukuminen/verenvuoto, 2/25 (8 %) hematoomia<br><br>Tapahtumataajuus yhteensä 19 %      |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022) | 2022 / Terumo Medical Corporation | Prospektiivinen, havainnoiva, markkinoille saattamisen jälkeinen monikeskustutkimus | Tarkoituksena on osoittaa FemoSeal™ VCS:n turvallisuus ja teho yhteisen reisivaltimon hemostaasin aikaansaamisessa todellisissa tilanteissa henkilöillä, joille suoritetaan perkutaanisia endovaskulaarisia toimenpiteitä.                                                                                                                                                                                                                                            | <ul style="list-style-type: none"> <li>Potilaan seuranta 30 päivän kohdalla (± 7 päivää) sairaalakäynnillä tai puhelinsoitolla.</li> <li>Tutkimukseen ottaminen: joulukuun 2021 ja heinäkuun 2022 välisenä aikana.</li> <li>230 tutkimukseen otettua tutkittavaa, joille suoritetaan diagnostinen tai interventionaalinen suonensisäinen toimenpide, jossa käytetään FemoSeal™-laitetta.</li> </ul> 3 tutkimuspaikkaa Euroopassa: Ranska (92 potilasta), Saksa (38 potilasta), Belgia (100 potilasta). | <ul style="list-style-type: none"> <li><b>Demografiset tiedot / samanaikaiset sairaudet:</b></li> <li>- Sukupuoli: 161 miestä (70 %) / 69 naista (30 %).</li> <li>- Keskimääräinen ikä: 70 ± 12.</li> <li>- BMI: 26,1 ± 4,95 kg/m<sup>2</sup>.</li> <li>- Hypertensio: 160 potilasta (69,6 %).</li> <li>- Dyslipidemia: 128 (55,7 %).</li> <li>- Sepelvaltimotauti: 42 (18,3 %).</li> <li>- Nykyinen tupakoitsija: 86 (37,6 %).</li> <li>- Tupakoinut aiemmin: 66 (28,8 %).</li> <li>- Sepelvaltimotauti: 34 (14 %).</li> <li>- Aiempi sydäninfarkti: 18 (7,8 %).</li> </ul> |

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|  |  |  |  |  | <ul style="list-style-type: none"> <li>- Ääreisvaltimon revaskularisaatio: 12 (5,2 %) kaulavaltimo ja 83 (37,5 %) ja alaraajan valtimo.</li> <li>- Antitrombosyyttihoito (lähtötasolla): 211 (91,7 %), mukaan lukien 21 (9,1 %) kaksoisverihiutaleestoitoa (DAPT).</li> <li>- Suun kautta otettava antikoagulaatio: 40 (17,4 %) potilasta.</li> <li>• <b>Toimenpiteiden ominaisuudet:</b> <ul style="list-style-type: none"> <li>- Ympäristö: sairaalahoitossa 162 potilasta (70,4 %), avohoidossa 68 potilasta (29,6 %).</li> <li>- Vallitseva indikaatio: katkokävely 147 potilasta (63,9 %).</li> <li>- Menetelmä: 35 anterogradisesti (15,3 %), 194 retrogradisesti (84,7 %).</li> </ul> </li> <li>• <b>Ensisijaiset päätetapahtumat:</b> <ul style="list-style-type: none"> <li>- Yhdistetty turvallisuuden (ei merkittäviä komplikaatioita sisäänvientikohdan raajassa 6 tunnin kuluessa toimenpiteestä) ja tehon (onnistunut pistokohdan hemostaasi) päätetapahtuma saavutettiin 215/226 (95,1 %) [95 % CI: 91,46; 97,55] potilaalla koko analyysiryhmässä ja 215/230 (93,5 %) [95 % CI 89,47, 96,30] potilaalla FemoSeal™-laitteella hoidetussa ryhmässä.</li> <li>- Tehon päätetapahtuma saavutettiin 219/226 (96,9 %) potilaalla, CI [93,7, 98,7].</li> </ul> </li> </ul> |
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|  |  |  |  |  | <p>- Turvallisuuden päätetapahtuma saavutettiin 220/230 (95,2 %) [95 % CI: 92,15, 97,90] potilaalla.</p> <p>• <b>Toissijaiset päätetapahtumat:</b></p> <p>- Ei lieviä sisäänvientikohdan komplikaatioita kuuden tunnin ajan toimenpiteen jälkeen 225/230 (97,8 %) potilaalla [95 %:n luottamusväli: 95,00; 99,29].</p> <p>- 219/230 potilaalla (95,2 %) [95 % CI: 91,60; 97,59] ei esiintynyt vakavia eikä lieviä sisäänvientikohdan komplikaatioita kuuden tunnin ja 30 päivän välisenä aikana toimenpiteen jälkeen.</p> <p>- Mediaaniaika hemostaasiin FemoSeal™ VCD:llä: 0,42 (0,25; 0,50) minuuttia.</p> <p>- Keskimääräinen aika liikkumiseen: 5,00 (4,54; 5,50) minuuttia.</p> <p>- Keskimääräinen sairaalassaoloaika: 23,98 (22,72, 25,00) tuntia.</p> <p>- FemoSeal™ VCS:n käytettävyys: "helppo" tai "erittäin helppo" aktivointi 98,7 %:ssa tapauksista ("helppo" aktivointi 21:ssa (9,2 %), "erittäin helppo" aktivointi 205:ssä (89,5 %)), ei lainkaan tai vähäistä vastusta aktivoinnissa 226:ssa (98,3 %) tapauksessa.</p> <p>152/230 (66,1 %) potilaista, joita hoidettiin FemoSeal™-pakkaukseen sisältyvällä johtimella (GW 0,038") ja joita suositellaan FemoSeal™-</p> |
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|  |  |  |  |  | laitteelle ilman raportoituja<br>laitevikoja tai<br>haittatapahtumia. |
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Vuonna 2006 toteutetussa tutkimuksessa pyrittiin varmistamaan nykyisen laitteen turvallisuus ja tehokkuus parannetulla toimitusjärjestelmällä sekä palautteen saaminen FemoSeal™ VCS:n käyttöohjeista ja koulutusohjelmasta. Tutkimukseen osallistui 100 potilasta, ja ensisijainen päätetapahtuma oli, oliko hemostaasi saavutettu tai tarvittiinko manuaalista tai mekaanista lisäkompressiota. Tutkimuksessa todettiin, että FemoSeal™-järjestelmän käyttö onnistui useimmissa tapauksissa (91 % saavutettiin välitön hemostaasi).

Vuoden 2008 tutkimuksessa oli 50 potilasta, ja siinä arvioitiin FemoSeal™-laitteen turvallisuutta ja suorituskykyä, kun sitä käytettiin normaalin klinisen rutiinin yhteydessä potilailla, joille tehtiin katetrointi 7F-holkilla. Tutkimuksen ensisijaisena päätetapahtumana oli kerätä tietoa hemostaasiajasta ja liikkeellelähetyksestä ilman lisäkompressiota, manuaalista tai mekaanista. Tutkimustulosten mukaan keskimääräinen hemostaasiaika oli 57,8 sekuntia ja kaikki potilaat pystyivät liikkumaan 4 tunnin vuodelevon jälkeen.

Vuoden 2009 tutkimuksessa arvioitiin uutta FemoSeal™ VCS -pakkausta. Tutkimuksessa oli 25 potilasta. Ensisijainen päätetapahtuma oli se, kokiko käyttäjä pakkauksen kanssa ongelmia. Käyttäjillä ei ollut ongelmia uuden FemoSeal™ VCS -pakkauksen kanssa. Tutkimuksessa kerättiin tietoa myös hemostaasiajasta.

Vuoden 2022 tutkimuksen tarkoituksena oli ennakoivasti kerätä tietoa koskien FemoSeal VCS:n turvallisuutta ja tehoa yhteisen reisivaltimon hemostaasin aikaansaamisessa todellisissa tilanteissa henkilöillä, joille suoritetaan perkutaanisia endovaskulaarisia toimenpiteitä. Tutkimuksessa oli 230 potilasta. Seurantatutkimuksen ensisijaiset päätetapahtumat ovat toimenpiteen onnistuminen (ts. onnistunut punktiokohdan hemostaasi) ja merkittävien komplikaatioiden väheneminen (esim. vaskulaarinen vamma, sisäänvientikohdan verenvuoto, sisäänvientikohdan infektio, toistuva manuaalinen kompressio ja uusi sisäänvientikohtaan liittyvä akuutti ipsilateraalinen jalan iskemia). Tutkimuksessa todettiin, että FemoSeal™ VCS toimii hyvin todellisissa tilanteissa ja mahdollistaa tehokkaan hemostaasin ja alhaisen sisäänvientikohdan komplikaatioiden määrän potilailla, joille tehdään perifeerisiä endovaskulaarisia toimenpiteitä. Sen suorituskyky osoittautui hyväksi, ja hemostaasin saavuttamiseen tarvittava aika oli lyhyt. Lisäksi käyttäjiltä saatiin hyvää palautetta sen käytettävyydestä. Siten FemoSeal™ VCS on arvokas laite reisivaltimoyhteyden sulkemiseen.

### 1.4.3 Tiivistelmä markkinoille saattamisen jälkeen toteutetusta seurannasta

#### 1.4.3.1 Toteutuneet markkinoille saattamisen jälkeiset kliiniset seurantatutkimukset

Yhteenveto markkinoille saattamisen jälkeisestä kliinisestä seurannasta on alla olevassa taulukossa 1.7.

**Taulukko 1.7. Kliiniset seurantatoimet markkinoille saattamisen jälkeen**

| Markkinoille saattamisen jälkeen toteutetut kliiniset tutkimukset         |             |                                                                                  |                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
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| Tutkimuksen nimi                                                          | Vuosi/CI    | Tutkimuksen tyyppi                                                               | Tavoitteet                                                                                                                                                                        | Välitavoitteet                                                                                                                                                                                                                                                                                                             | Mahdolliset hyväksymiskriteerit                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021<br>TMC | Markkinoille saattamisen jälkeinen kliininen tutkimus – korkealaatuinen tutkimus | Markkinoille saattamisen jälkeinen kyselytutkimus, jolla kerätään tulevaa palautetta Euroopan unionin markkinoilla myytävän FemoSeal™ Vascular Closure Device -laitteen käytöstä. | <ul style="list-style-type: none"> <li>120 tapausta</li> <li>8 lääkäriä, joilla on yli 5 vuoden kokemus</li> <li>Useita Euroopan maita</li> </ul>                                                                                                                                                                          | <b>Laitteen arviointi asteikolla 1–5 – kyselyn lausunnot</b> <ul style="list-style-type: none"> <li>Hyväksymiskriteerit               <ul style="list-style-type: none"> <li>Arvosanat 3–5 katsotaan suotuisiksi</li> <li>Kaikissa lausunnoissa tuli olla ≥ 80 %:sti myönteistä palautetta</li> </ul> </li> <li>Tulokset               <ul style="list-style-type: none"> <li>Yhdenkään kyselyn lausunnoissa ei ollut yli 20 % epäsuotuisia vastauksia</li> <li>Tuotteesta ei ole täytetty reklamaatioilmoituksia</li> </ul> </li> </ul> |
| 20210298 – 0.035” and 0038” Guidewire Clinical Survey Report (2021)       | 2021<br>TMC | Markkinoille saattamisen jälkeinen kliininen tutkimus – korkealaatuinen tutkimus | Markkinoille saattamisen jälkeinen kysely, jossa kerätään pitkän aikavälin palaute 6 Fr Angio-Seal™ VIP Vascular Closure Device (VCD) -sulkulaitteen                              | <ul style="list-style-type: none"> <li>Kyselyt 0,035” ohjainlangalle               <ul style="list-style-type: none"> <li>106 kyselyä</li> <li>64 lääkäriä</li> </ul> </li> <li>Kyselyt 0,038” ohjainlangalle               <ul style="list-style-type: none"> <li>109 kyselyä</li> <li>55 lääkäriä</li> </ul> </li> </ul> | <b>Laitteen arviointi asteikolla 1–5 – kyselyn lausunnot</b> <ul style="list-style-type: none"> <li>Hyväksymiskriteerit               <ul style="list-style-type: none"> <li>Arvosanat 3–5 katsotaan suotuisiksi</li> <li>Kaikissa lausunnoissa</li> </ul> </li> </ul>                                                                                                                                                                                                                                                                   |

| Markkinoille saattamisen jälkeen toteutetut kliiniset tutkimukset                                                               |                     |                                                                                  |                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|---------------------------------------------------------------------------------------------------------------------------------|---------------------|----------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                 |                     |                                                                                  | mukana toimitetun 0,035 tuuman johtimen ja sekä 8 Fr Angio-Seal™ VIP VCD -sulkulaitteen että FemoSeal Vascular Closure System -sulkujärjestelmän mukana toimitetun 0,038 tuuman johtimen käytöstä Euroopan unionin markkinoilla. | <ul style="list-style-type: none"> <li>12 takautuvaa kyselyä</li> </ul>                                                                                                                                                                                                                                        | a tuli olla ≥ 80 %:sti myönteistä palautetta <ul style="list-style-type: none"> <li>Tulokset             <ul style="list-style-type: none"> <li>Kaikki ohjainlangat saivat hyväksyttävän luokituksen</li> <li>Tuotteesta ei täytetty reklamaatioilmoituksia</li> </ul> </li> </ul>                                                                                                                                                                                                                                                                                       |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023–2024<br>TMC/TE | Markkinoille saattamisen jälkeinen kliininen tutkimus – korkealaatuinen tutkimus | Kerätä seurantana palautetta FemoSeal VCS:n käytöstä EU-markkinoilla myytävien ohjainlankojen kanssa.                                                                                                                            | <ul style="list-style-type: none"> <li>126 kyselyä</li> <li>7 tutkimuspaikkaa</li> <li>5 maata</li> <li>14.11.2023–11.6.2024</li> <li>Lääkärin erikoistumisala:             <ul style="list-style-type: none"> <li>Verisuonikirurgia</li> <li>Toimenpide radiologia</li> <li>Angiologia</li> </ul> </li> </ul> | <b>Laitteen arviointi 5-portaisella asteikolla – kyselyn lausunnot</b> <ul style="list-style-type: none"> <li>Hyväksymiskriteerit             <ul style="list-style-type: none"> <li>Arvosanat 3–5 katsotaan suotuisiksi</li> <li>Kaikissa lausunnoissa tuli olla ≥ 80 %:sti myönteistä palautetta</li> <li>Jos tässä kyselyssä ilmenee haittatahtumia, niiden tulisi olla riskienhallinnan ennakoimia tapahtumia.</li> </ul> </li> <li>Potilaiden demografiset tiedot             <ul style="list-style-type: none"> <li>Nainen: 29,4 % (37/126)</li> </ul> </li> </ul> |

| Markkinoille saattamisen jälkeen toteutetut kliiniset tutkimukset |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|-------------------------------------------------------------------|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                   |  |  |  |  | <ul style="list-style-type: none"> <li>○ Mies:<br/>69,8 %<br/>(88/126)</li> <li>○ Sukupuolta ei mainittu:<br/>0,8 (1/126)</li> <li>○ Ikä &gt; 75 vuotta:<br/>31,7 %</li> <li>• Tulokset               <ul style="list-style-type: none"> <li>○ FemoSeal™ VCS:n mukana toimitettu ohjainlanka:<br/>101/126 (80,2 %).</li> <li>○ Toimenpiteen kesto (minuutteja):<br/>63,4 (36,6) (keskiarvo (keskihajonta)); 57,0 (36,0–81,0) (mediaani (IQR))</li> <li>○ Kaikki FemoSeal™ VCS:n suorituskyky luokitukset olivat positiivisia.</li> <li>○ Kaikki FemoSeal™ VCS:n mukana toimitetun ohjainlangan luokitukset olivat positiiviset.</li> <li>○ Yksi haittatapahtuma (0,8 %):<br/>FemoSeal™ VCS -levyt eivät olleet</li> </ul> </li> </ul> |

| Markkinoille saattamisen jälkeen toteutetut kliiniset tutkimukset |  |  |  |  |                                                                                                                                                                                                                                                        |
|-------------------------------------------------------------------|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                   |  |  |  |  | hyvin<br>kohdistettuna<br>luultavasti<br>jäykän johtimen<br>(Boston<br>Scientific<br>Amplatz Super<br>Stiff, 75 cm,<br>0,035 tuumaa)<br>käytön vuoksi,<br>minkä vuoksi<br>manuaalista<br>kompressiota<br>vaadittiin<br>hemostaasin<br>saavuttamiseksi. |

Terumo Medical Corporation on toteuttanut kolme korkealaatuista lääkärikäyttäjille tehtyä tutkimusta kuluvalle raportointikaudella (1.9.2019–31.8.2024).

FemoSeal™-laitteen kliinisissä tutkimuksissa kerättiin proaktiivista kliinistä tietoa FemoSeal™ VCS -laitteen turvallisuudesta ja suorituskyvystä kliinisen käytön aikana. Tutkimukseen sisältyi kysymyksiä koko laitteesta ja siihen liittyvistä lisävarusteista, kuten 0,038" johtimesta, ja niiden välittömästä vuorovaikutuksesta. Johdinta koskevissa kliinisissä tutkimuksissa on kerätty ennakoivia kliinisiä tietoja FemoSeal™-laitteen mukana toimitetun 0,038" johtimen turvallisuudesta ja suorituskyvystä kliinisen käytön aikana. Kyselyssä keskityttiin erityisesti johtimen yleiseen käyttöön aina sisäänviennistä toimenpideholkin kautta verisuonistoon ja johtimen poistamiseen.

FemoSeal™ VCS -laite ja sen mukana toimitettava 0,038" johdin saivat hyväksytyt luokitukset, ja kuusi (6) reklamaatiota tehtiin laitteesta ja yhdeksän (9) ei-reklamaatiota johtimesta korkealaatuista kliinisistä tutkimuksista saatujen kommenttien arvioinnin perusteella. Reklamaatiot on arvioitu sekä FemoSeal-laitteen että johtimen osalta, ja ne arvioitiin osana Terumon markkinoille tulon jälkeistä valvontaprosessia. Uusia riskejä ja/tai riskitasoja ei tunnistettu.

Osana markkinoille saattamisen jälkeistä kliinistä tutkimusta toteutettiin vuonna 2024 lääkärikäyttäjille suunnattu tutkimus. Tutkimuksen tulokset osoittivat, että FemoSeal™ VCS:n suorituskky ja turvallisuus olivat yleisesti ottaen hyvin positiiviset. Myös muiden kuin FemoSeal™ VCS:n mukana toimitettujen ohjainlankojen yhteensopivuus osoitettiin.

#### 1.4.3.2 Jatkuva tai suunniteltu markkinoilletulon jälkeinen kliininen seuranta

TMC:llä on yksi meneillään oleva/suunniteltu markkinoille tulon jälkeinen kliininen seurantatoiminto. Kliininen kysely, jolla kerätään pitkän aikavälin palautetta johtimen käytöstä EU-markkinoilla myydyn FemoSeal VCS -laitteen kanssa, toteutetaan. Lääkärit vastaavat kyselyyn, ja vastausten pohjalta tutkitaan, mitä johtimia he käyttivät toimenpiteen aikana. Tämän kyselyn tarkoituksena on korjata puute, joka on tunnistettu kirjallisuuden ja ulkoisten arvioijien antamien kommenttien puuttumisena FemoSeal™ VCS:n yhteensopivuudesta muiden kuin Terumo-merkkisten ohjainlankojen kanssa. Palaute koskee teknisiä tuloksia, kliinistä suorituskkyä ja laitteen suorituskkyyn liittyvää turvallisuutta erilaisilla johtimilla.

#### 1.4.4 Systemaattisen kirjallisuuskatsauksen yhteenveto

Terumo Medical Corporation tekee systemaattisia kirjallisuuskatsauksia FemoSeal™ VCS -laitetta ja/tai vastaavia laitteita koskevista julkaistuista tutkimuksista kerätäkseen ja arvioidakseen laitteen kliinisiä turvallisuus- ja suorituskkytietoja. Julkaistun kirjallisuuden vuosittaisen seulonnan tavoitteena on tunnistaa aiemmin tuntemattomat haittavaikutukset, seurata tunnettuja haittavaikutuksia, tunnistaa mahdolliset vaaratilanteet ja tunnistaa mahdollinen FemoSeal™ VCS -laitteen systemaattinen väärinkäyttö tai myyntiluvasta poikkeava käyttö.

Tuoreimmassa systemaattisessa kirjallisuuskatsauksessa, joka koski ajanjaksoa 1.9.2019–31.8.2023, tunnistettiin 29 julkaistua tutkimusta, joissa oli FemoSeal™ VCS -laitteen kliinisiä turvallisuutta ja tehoa koskevia tietoja. Kaksikymmentäkolme referenssiä raportoi FemoSeal™ VCS:n myyntiluvan mukaisesta käytöstä ja yhdeksän tutkimusta raportoi myyntiluvasta poikkeavasta käytöstä. Nimenomaan FemoSeal™ VCS:n käyttöä koskevista tutkimuksista ilmenee tutkimuspopulaatio, joka on edustava EU:n alueella potilaiden osalta, joille suoritetaan perkutaanisia katetrointitoimenpiteitä. **Kohdassa 3** on luettelo näistä 23 vertaisarviodusta julkaisusta.

Kliinistä suorituskkyä arvioitiin seuraavilla mittareilla:

- Hemostaasiaika on parempi tai verrannollinen normaaliin reisivaltimon perkutaanisen sulkemistoimenpiteen uusimpaan tekniikkaan.
- Liikkeellelähtöaika on parempi tai verrattavissa normaaliin reisivaltimon perkutaanisen sulkemismenetelmän uusimpaan tekniikkaan.
- Leikkauksen jälkeisten komplikaatioiden määrä on alhaisempi tai verrannollinen nykyisiin hoitostandardeihin.

Näiden kliinisten suorituskkymittareiden perusteella kirjallisuuskatsauksen tiedot osoittivat, että FemoSeal™ VCS -laitetta voidaan käyttää onnistuneesti reisivaltimopunktion (arteriotomian) sulkemiseen potilailla, joille on suoritettu perkutaaninen katetrointi käyttämällä 7 Fr:n tai pienempää toimenpidetähtä. Täydellinen hemostaasi saavutettiin useimmilla potilailla (79,65–100 %), ja siihen liittyi 0,5 minuutin mediaani hemostaasiaika ja 3 päivän mediaaniaika

kotiutukseen. 69,2–86,7 % potilaista pystyi liikkumaan 5 tuntia valtimon sulkemisen jälkeen, ja leikkauksen jälkeinen keskimääräinen paras aika oli 349 minuuttia. FemoSeal™ VCS:n pettämistä havaittiin 3,68–4 %:ssa tapauksista, ja manuaalista lisäkompressiota tarvittiin 0,9–4,4 %:ssa toimenpiteistä.

Kliinistä turvallisuutta arvioitiin haittavaikutusten perusteella, mukaan lukien muun muassa seuraavat:

- Verenvuoto
- Hematooma
- Valeaneurysma
- Ruhje
- Valtimo-laskimofisteli
- Infektio
- Kuolema

Näiden haittatapahtumien FemoSeal™ VCS -laitteelle ilmoitettu esiintyvyys katsaukseen kuuluvissa tutkimuksissa oli pienempi tai verrattavissa aiempiin, manuaalista kompressiota ja muita verisuonensulkulaitteita koskeviin raportoituihin esiintyvyyksiin.

Haittatapahtumia ei havaittu 10 tapausraportin katsauksessa, koska uusia, odottamattomia, kehittymässä olevia tai ei-hyväksyttäviä riskejä ei havaittu.

FemoSeal™ VCS:n käytön yleinen toimintateho diagnostisen angiografian tai interventiotoinenpiteiden aikana riippuu useista tekijöistä, kuten potilaan sukupuolesta, iästä, anatomiasta, samanaikaisista sairauksista, punktiokohdan anatomisesta sijainnista, kirurgin kokemuksesta, VCD:n asennusmenetelmästä, leikkauksen jälkeisestä hoidosta jne. FemoSeal™ VCS:n teknisen menestyksen, mukaan lukien hemostaasin saavuttamisen, lisäksi se mahdollisti verisuonten sulkemiseen liittyviä kliinisiä hyötyjä reisivaltimon punktion jälkeen, kuten nopeamman hemostaasiajan ja nopeamman liikkeelleläähtöajan. FemoSeal™ VCS -laitteiden suorituskykytulokset ovat yhdenmukaisia tämän tyyppiseltä laitteelta odotettavien tulosten kanssa, kun sitä käytetään käyttötarkoituksen mukaisesti. Osa nykyisen tutkimusjakson aikana haetuista referensseistä osoitti tutkittavaa laitetta käytetyn muussa anatomisessa sijainnissa kuin yhteisessä reisivaltimossa ja > 7F:n arteriotomioiden sulkemisessa, mikä katsotaan myyntiluvasta poikkeavaksi toimenpiteeksi.

Katsauksen yhteydessä ei tunnistettu tuntemattomia haittavaikutuksia, mahdollisia vaaratilanteita tai laitteen mahdollista systemaattista väärinkäyttöä. Jos koulutetut lääkärit käyttävät FemoSeal™ VCS -laitetta huolellisesti, lääkinnällinen laite toimii hyödyllisenä ja olennaisena kliinisenä laitteena. Kaiken kaikkiaan kohdehoito ja siten FemoSeal™ VCS vastaavat nykyisiin kliinisiin tarpeisiin suoniyhdyteen liittyvien komplikaatioiden hoidossa.

Kaiken kaikkiaan kirjallisuuskatsauksessa ei havaittu kliinisissä olosuhteissa mitään suorituskykyä tai turvallisuutta koskevia ongelmia, jotka olisivat olleet aiemmin tuntemattomia, tai haittavaikutuksia, joita olisi esiintynyt odotettua suurempia/hyväksyttäviä määriä. Siksi kirjallisuuskatsauksen perusteella voidaan todeta, että kun FemoSeal™ VCS -laitetta käytetään kompressioon arteriotomiassa perkutaanisen katetroinnin jälkeen, se toimii edelleen odotetulla tavalla eikä siihen liity vakavia turvallisuustapahtumia.

#### 1.4.5 Tiivistelmä markkinoille saattamisen jälkeisestä valvonnasta

Käytössä on ennakkoiva markkinoille saattamisen jälkeisen valvonnan järjestelmä, ja kaikki reklamaatiot arvioidaan kuukausittain sisäisten valmistustoimenpiteiden mukaisesti. Reklamaatiotiedot analysoitiin ajalta 1.9.2019–31.8.2024. Valmistajalle lähetettiin kaiken kaikkiaan 28 lääkinnällisten laitteiden vaaratilanneilmoitusta (Medical Device Vigilance (MDV) Report) ja 476 asiakasreklamaatiota. 28 MDV-raportista 27 liittyi haittavaikutuksiin ja yksi laitteen toimintahäiriöön. Raportointijakson aikana tapahtui kaksi kuolemantapausta, mutta kumpikaan raportoiduista kuolemantapauksista ei liittynyt tutkimuslaitteeseen. Valmistajalle tehdyistä 476 reklamaatiosta yleisin syy reklamaatioon oli käyttöönottovaikeudet (146 esiintymää, esiintymistiheys 0,0142). Toiseksi yleisin vika on laitteen tulo ulos vedettäessä, ja sen osuus on 0,0126 % (130 tapahtumaa).

FemoSeal™ Vascular Closure Systemin myynti on maailmanlaajuisesti 1 030 136 kappaletta ja Euroopan talousalueella 827 843. Laskennallinen reklamaatiotiheys on maailmanlaajuisen myynnin perusteella 0,046 %. Asiakasreklamaatioiden osuus on hyvin pieni. Mitään sellaisia uusia riskejä ei tunnistettu, jotka eivät jo sisälly käyttöohjeisiin ja riskidokumentaatioon.

Haittavaikutusten esiintymistiheydet on esitetty **taulukossa 1.2**. Uusia odottamattomia, kehittyvässä olevia tai ei-hyväksyttäviä riskejä ei reklamaatioista havaittu. Tunnettujen haittavaikutusten esiintymistiheydessä tai vakavuudessa ei havaittu merkittävää nousua.

#### 1.4.6 Kliinistä suorituskykyä ja turvallisuutta koskeva kokonaistiivistelmä

FemoSeal™ VCS on tarkoitettu yhteisen reisivaltimon punktion (arteriotomian) sulkemiseen potilailla, joille on suoritettu perkutaaninen katetrointi käyttämällä enintään 7F (2,33 mm) - kokoista toimenpideholkkia. Tämä kliininen arviointi perustuu kattavaan analyysiin saatavilla olevista markkinoille saattamista edeltävistä ja markkinoille saattamisen jälkeisistä kliinisistä tiedoista ja kirjallisuudesta, jotka liittyvät FemoSeal™ VCS:n käyttötarkoitukseen.

Julkaistua kirjallisuutta tarkasteltiin kattavasti 1. syyskuuta 2019 ja 31. elokuuta 2024 väliseltä ajalta. Näyttöaineistoon sisältyi 29 FemoSeal™ VCS:ää koskevaa tutkimusta. Kliinisessä arvioinnissa esitetyn näytön perusteella voidaan päätellä, että käyttöaiheen mukaisesti käytettynä tutkittava laite on turvallinen ja tehokas ja että kaikki riskit tai ei-toivotut haittavaikutukset, jotka voivat liittyä laitteeseen normaaleissa käyttöolosuhteissa, ovat hyväksyttäviä riskejä, kun niitä verrataan hyötyihin potilaalle. Tutkittavien laitteiden suorituskykytulokset ovat yhdenmukaisia



tämän tyyppiseltä laitteelta odotettavien tulosten kanssa, kun sitä käytetään käyttötarkoituksen mukaisesti.

FemoSeal™ VCS -laitteen käyttöön liittyviä mahdollisia haittavaikutuksia ovat muun muassa haittavaikutukset, joita on yleisesti raportoitu vaihtoehtoisten arteriotomiasulkumenetelmien yhteydessä, esim. verenvuoto ja hematooma. Kaiken kaikkiaan FemoSeal™ VCS -laitteen käytön yhteydessä raportoitujen haittavaikutusten esiintyvyydet ovat samankaltaisia kuin manuaalisella kompressiolla ja vastaavilla verisuonisulkulaitteilla raportoidut esiintyvyydet. Verenvuodon ja hematooman ilmoitetut esiintyvyydet ovat kuitenkin FemoSeal™ VCS -laitteella pienempiä kuin ilmoitetut esiintyvyydet samankaltaisilla verisuonisulkulaitteilla. Jokainen ilmoitettu haittavaikutus, sekä julkaistussa kirjallisuudessa että markkinoille tulon jälkeisessä seurannassa, oli aiemmin tunnistettu (katso **kohta 1.3**).

Olemassa olevat tiedot FemoSeal VCS:n kliinisestä turvallisuudesta ja suorituskyvystä viittaavat siihen, että kyseisen verisuonisulkulaitteen käytöstä potilaalle koituvat hyödyt ovat mahdollisia riskejä suuremmat, kun sitä käytetään käyttöohjeiden mukaisesti.

Kuten edellisessä osassa mainittiin, FemoSeal™ VCS -laitteen tiedot osoittavat yhdenmukaisuuden arvioitavaan laitteeseen liittyvien tietojen (esim. laitteen käyttö, turvallisuutta koskevat tulokset, kliininen suorituskky ja kliiniset hyödyt) välillä, tunnistettujen vastaavien laitteiden ja vastaaviin laitteisiin liittyvien tietojen välillä, jotka mainitaan uusimman tekniikan mukaisten laitteiden luettelossa.

Turvallisuustietojen poikittaisanalyysissä ei puutteita havaittu seuraavien välillä:

- Nykytekniikan mukaiset tiedot
- Arvioitavaan laitteeseen liittyvät tiedot
- Riskienhallintatiedoissa mainitut tiedot
- Merkinnöissä ja/tai käyttöohjeissa mainitut tiedot (eli käyttäjälle siirtyvät jäljelle jääneet riskit on käsitelty).

Kliininen turvallisuus on osoitettu alhaisella määrällä komplikaatioita, jotka on havaittu julkaistussa vertaisarvioidussa kliinisessä kirjallisuudessa, yrityksen rahoittamissa kliinisissä tutkimuksissa, markkinoille saattamisen jälkeen saatujen tietojen tarkasteluissa, joissa ei ole mainintoja myyntilupien peruuttamista. Suorituskvyyssä ei ole havaittu ongelmia. Tutkitussa kirjallisuudessa FemoSeal™ VCS -laitetta oli käytetty valmistajan käyttötarkoituksen mukaisesti.

## 1.5 Mahdolliset diagnostiset tai terapeutiset vaihtoehdot

Manuaalista kompressiota käytetään perinteisesti hemostaasin aikaansaamiseen arteriotomikohdassa verisuonikatetroinnin jälkeen. Manuaaliseen kompressioon on liittynyt se, että potilas joutuu olemaan liikkumatta pitkiä aikoja (jopa 8 tuntia toimenpiteen jälkeen), potilas kokee huomattavaa epämukavuutta ja sairaalassaoloaika on pidentynyt. Äskettäisen systemaattisen kirjallisuuskatsauksen mukaan hemostaasin saavuttamiseen kuluvan ajan mediaani oli manuaalisella kompressiolla 20,8 minuuttia.<sup>1</sup>

Manuaalisen kompression sijasta voidaan käyttää ulkoisia hemostaasilaitteita, jotka kohdistavat arteriotomiakohtaan mekaanisen kompression. Nämä laitteet eivät lyhennä hemostaasiaikaa tai liikkumaan pääsyä, mutta ne vähentävät henkilökunnan tarvetta korvaamalla manuaalisen kompression mekaanisella kompressiolla. Mekaaniseen kompressioon liittyvät haittatapahtumat ovat samankaltaisia kuin manuaalisessa kompressiossa.

Verisuonensulkulaitteet, kuten FemoSeal™ VCS, on suunniteltu arteriotomian sulkemiseen. Niiden tarkoituksena on lyhentää hemostaasiin kuluvaa aikaa ja mahdollistaa aikaisempi liikkumaan pääsy. Äskettäin tehdyssä systemaattisessa kirjallisuuskatsauksessa, johon sisältyi 13 yleisesti saatavilla olevaa laitetta, havaittiin, että hemostaasin saavuttamiseen kuluvan ajan mediaani verisuonten sulkulaitteella oli 5,4 minuuttia. Yksittäisten verisuonensulkulaitteiden hemostaasiajan mediaani vaihteli 1 minuutista (FemoSeal™ VCS) 14 minuuttiin, ja valtaosalla laitteista se oli 4–10 minuuttia.<sup>1</sup>

Arteriotomikohdan sulkemiseen liittyviä yleisiä haittatapahtumia manuaalisen kompression, ulkoisen hemostaasilaitteen ja verisuonensulkulaitteen käytön yhteydessä ovat hematooma, verenvuoto sisäänvientikohdassa, pseudoaneurysma, arteriovenoosinen fisteli ja infektio. Samassa järjestelmällisessä katsauksessa (34 satunnaistettua kontrolloitua tutkimusta, 14 401 potilasta) havaittiin, että haittavaikutusten määrät olivat samankaltaisia manuaalisen kompression ja verisuontensulkulaitteiden käytön välillä, paitsi että verenvuoto oli yleensä hieman suurempi verisuontensulkulaitteiden kanssa.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Ehdotettu käyttäjäprofiili ja koulutus

FemoSeal™ Vascular Closure Systemin suunnitellut käyttäjät ovat lääkäreitä, joilla on koulutus valtimoyhteyden avaamiseen ja sulkemiseen endovaskulaarisissa toimenpiteissä yhteisen reisivaltimon kautta ja jotka ovat osallistuneet Terumo Medical Corporationin lääkäreille tarkoitettuun FemoSeal™-opetusohjelmaan.

## 1.7 Asiaankuuluvat yhdenmukaistetut ja yleiset standardit

| Standardiviite | Nykyinen vaatimustenmukaisuusvuosi/versio | Kuvaus                                                                                                                                   |
|----------------|-------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070      | 2014/AMD1:2018                            | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070   | 2014/A1:2018                              | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance   | 20. toukokuuta 2021                       | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052     | 2015                                      | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213     | 2017                                      | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503     | 2020                                      | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182     | 2019                                      | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |
| EN ISO 13485   | 2016/A11:2021                             | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 13485      | 2016                                      | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 14644-1    | 2015                                      | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                  |
| EN ISO 14644-1 | 2015                                      | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                  |

| Standardiviite             | Nykyinen vaatimustenmukaisuusvuosi/versio | Kuvaus                                                                                                                                                                   |
|----------------------------|-------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14644-2                | 2015                                      | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2             | 2015                                      | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3                | 2019                                      | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3             | 2019                                      | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1                | 2003                                      | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1             | 2003                                      | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2                | 2003/TC1:2004                             | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| EN ISO 14698-2             | 2003/TC 1:2004                            | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| USP <788>                  | N/A                                       | PARTICULATE MATTER IN INJECTIONS                                                                                                                                         |
| Euroopan farmakopea 2.9.19 | N/A                                       | Particulate Contamination: Sub-Visible Particles                                                                                                                         |
| IEC 62366-1                | 2015                                      | Medical devices — Part 1: Application of usability engineering to medical devices                                                                                        |

| Standardiviite | Nykyinen vaatimustenmukaisuusvuosi/versio | Kuvaus                                                                                                               |
|----------------|-------------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| EN 62366-1     | 2015                                      | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN ISO 14971   | 2019/A11:2021                             | Medical devices — Application of risk management to Medical devices                                                  |
| ISO 14971      | 2019                                      | Medical devices — Application of risk management to Medical devices                                                  |
| ASTM F1980     | 2016                                      | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1 | 2020                                      | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1    | 2018                                      | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2 | 2006                                      | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2    | 2006                                      | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3 | 2014                                      | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3    | 2014                                      | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4 | 2017                                      | Biological Evaluation of Medical Devices - Part 4: Selection of tests for interactions with blood                    |
| ISO 10993-4    | 2017                                      | Biological Evaluation of Medical Devices - Part 4: Selection of tests for interactions with blood                    |
| EN ISO 10993-5 | 2009                                      | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| ISO 10993-5    | 2009                                      | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |

| Standardiviite  | Nykyinen vaatimustenmukaisuusvuosi/versio | Kuvaus                                                                                                                                     |
|-----------------|-------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-6  | 2016                                      | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| ISO 10993-6     | 2016                                      | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| EN ISO 10993-10 | 2023                                      | Biological evaluation of medical devices - Part 10: Tests for irritation and skin sensitization                                            |
| ISO 10993-10    | 2021                                      | Biological evaluation of medical devices - Part 10: Tests for irritation and skin sensitization                                            |
| EN ISO 10993-11 | 2018                                      | Biological evaluation of medical devices - Part 11: Tests for systemic toxicity                                                            |
| ISO 10993-11    | 2017                                      | Biological evaluation of medical devices - Part 11: Tests for systemic toxicity                                                            |
| EN ISO 10993-12 | 2021                                      | Biological evaluation of medical devices - Part 12: Sample preparation and reference materials                                             |
| ISO 10993-12    | 2021                                      | Biological evaluation of medical devices - Part 12: Sample preparation and reference materials                                             |
| EN ISO 10993-17 | 2009                                      | Biological evaluation of medical devices - Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17    | 2002                                      | Biological evaluation of medical devices - Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18    | 2020/A1:2022                              | Biological evaluation of medical devices - Part 18: Chemical characterization of medical device materials within a risk management process |
| EN ISO 10993-18 | 2020/A1:2022                              | Biological evaluation of medical devices - Part 18: Chemical characterization of medical device materials within a risk management process |
| EN ISO 10993-23 | 2021                                      | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |

| Standardiviite | Nykyinen vaatimustenmukaisuusvuosi/versio | Kuvaus                                                                                                                                                                       |
|----------------|-------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-23   | 2021                                      | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382     | 2018                                      | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756      | 2017                                      | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>       | N/A                                       | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>      | N/A                                       | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72 | 2019                                      | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135   | 2014/A1:2019                              | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135      | 2014/A1:2018                              | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7 | 2008/A1:2022                              | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |
| ISO 10993-7    | 2008/A1:2019                              | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                                            |
| EN 556-1       | 2024                                      | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices              |

| Standardiviite | Nykyinen vaatimustenmukaisuusvuosi/versio | Kuvaus                                                                                                                                   |
|----------------|-------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 11737-1 | 2018/A1:2021                              | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products    |
| ISO 11737-1    | 2018/A1:2021                              | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products    |
| EN ISO 11138-1 | 2017                                      | Sterilization of health care products - Biological indicators - Part 1: General requirements                                             |
| ISO 11138-1    | 2017                                      | Sterilization of health care products - Biological indicators - Part 1: General requirements                                             |
| EN ISO 11138-2 | 2017                                      | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| ISO 11138-2    | 2017                                      | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| EN ISO 15223-1 | 2016                                      | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| ISO 15223-1    | 2016                                      | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| EN 1041        | 2008/A1:2013                              | Information supplied by the manufacturer of medical devices                                                                              |
| EN ISO 11607-1 | 2020/A1:2023                              | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| ISO 11607-1    | 2019/A1:2023                              | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |



| Standardiviite    | Nykyinen vaatimustenmukaisuusvuosi/versio | Kuvaus                                                                                                                                                                     |
|-------------------|-------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 11607-2    | 2020/A1:2023                              | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ISO 11607-2       | 2019/A1:2023                              | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169        | 2016                                      | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M | 2016                                      | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825        | 2018                                      | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096        | 2011 (R 2019)                             | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M     | 2015                                      | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24      | 2021                                      | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3       | 2020                                      | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |
| MDCG 2020-8       | 2020                                      | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                             |
| MDCG 2020-7       | 2020                                      | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                          |
| MDCG 2020-6       | 2020                                      | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                       |

| Standardiviite | Nykyinen vaatimustenmukaisuusvuosi/versio | Kuvaus                                                                                                                                                                                                                                                        |
|----------------|-------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2019-9 v1 | 2022                                      | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                                                                                      |
| MDCG 2019-8 v2 | 2020                                      | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15   | 2020                                      | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11   | 2021                                      | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19   | 2021                                      | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4 | 2021                                      | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2    | 2019                                      | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1    | 2019                                      | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7    | 2018                                      | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6    | 2018                                      | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |
| MDCG 2018-4    | 2018                                      | MDCG 2018-4 Annex: UDI database Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                                                                                                  |

| Standardiviite      | Nykyinen vaatimustenmukaisuusvuosi/versio | Kuvaus                                                                                                                                                                                        |
|---------------------|-------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2018-3 v1      | 2020                                      | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25        | 2021                                      | Regulation (EU) 2017/745 - application of MDR requirements to ‘legacy devices’ and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2.12-2 Rev 2 | 2012                                      | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                        |

## 2.0 KIRJALLISUUS

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### 3.0 MUUTOSHISTORIA

| SSCP-versionumero       | Julkaisupäivä        | Muutoksen kuvaus                                       | Ilmoitetun laitoksen vahvistama versio                                                                                                                                                                                                                                                                                                                                                        |
|-------------------------|----------------------|--------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022            | 20. tammikuuta 2023  | Ensimmäinen julkaisu, MDR CE -sertifioinnin yhteydessä | <input checked="" type="checkbox"/> Kyllä<br>Validointikieli: English<br><input type="checkbox"/> Ei (koskee vain luokan IIa tai joitakin IIb implantoitavia laitteita (MDR, 52 artikla 4 kohta 2. alakohta), jolle ei vielä ole ilmoitetun laitoksen vahvistamaa laitteen turvallisuutta ja kliinistä suorituskkyä koskevaa tiivistelmää (SSCP))<br><input type="checkbox"/> Muu (tarkenna): |
| SSCP-FS-2023 – Versio 1 | 15. maaliskuuta 2024 | Päivitetty 1.1.2019 ja 31.12.2023 väliselle ajalle.    | <input checked="" type="checkbox"/> Kyllä<br>Validointikieli: English<br><input type="checkbox"/> Ei (koskee vain luokan IIa tai joitakin IIb implantoitavia laitteita (MDR, 52 artikla 4 kohta 2. alakohta), jolle ei vielä ole ilmoitetun laitoksen vahvistamaa laitteen turvallisuutta ja kliinistä suorituskkyä koskevaa tiivistelmää (SSCP))<br><input type="checkbox"/> Muu (tarkenna): |
| SSCP-FS-2024 Versio 1   |                      | Päivitetty 1.9.2019 ja 31.8.2024 väliselle ajalle.     | <input type="checkbox"/> Kyllä<br>Validointikieli: English<br><input type="checkbox"/> Ei (koskee vain luokan IIa tai joitakin IIb implantoitavia laitteita (MDR, 52 artikla 4 kohta 2. alakohta), jolle ei vielä ole ilmoitetun laitoksen vahvistamaa laitteen turvallisuutta ja kliinistä                                                                                                   |

|                          |               |                                                            |                                                                                                                                                                                                                                                                                                                                                                                                        |
|--------------------------|---------------|------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                          |               |                                                            | suorituskykyä koskevaa tiivistelmää (SSCP))<br><br><input type="checkbox"/> Muu (tarkenna):                                                                                                                                                                                                                                                                                                            |
| SSCP-FS-2024<br>Versio 2 | June 20, 2025 | Tarkistettu NSAI-kyselyiden perusteella validointia varten | <input checked="" type="checkbox"/> Kyllä<br>Validointikieli: English<br><br><input type="checkbox"/> Ei (koskee vain luokan IIa tai joitakin IIb implantoitavia laitteita (MDR, 52 artikla 4 kohta 2. alakohta), jolle ei vielä ole ilmoitetun laitoksen vahvistamaa laitteen turvallisuutta ja kliinistä suorituskykyä koskevaa tiivistelmää (SSCP))<br><br><input type="checkbox"/> Muu (tarkenna): |



## Résumé des performances cliniques et de sécurité

### FemoSeal™ Vascular Closure System

|                                                       |                                                                                               |
|-------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| <b>Fabricant</b>                                      | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 USA           |
| <b>SRN du fabricant</b>                               | US-MF-000019594                                                                               |
| <b>Représentant de la direction/PRRC</b>              | Kimberly Feitl<br>Vice President, Quality                                                     |
| <b>Basic UDI-DI</b>                                   | 38970FS79                                                                                     |
| <b>Numéro EMDN</b>                                    | C900199 – Systèmes d’hémostase – Autre                                                        |
| <b>Classe du dispositif</b>                           | Classe III                                                                                    |
| <b>Année du premier marquage<br/>CE du dispositif</b> | 2005                                                                                          |
| <b>Représentant pour l’UE</b>                         | Terumo Europe N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgique<br>SRN : BE-AR-000001433 |
| <b>Organisme notifié</b>                              | NSAI<br>CE 0050                                                                               |

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Ce résumé des performances cliniques et de sécurité (SSCP) est destiné à donner accès au public à un résumé actualisé des principaux aspects des performances cliniques et de sécurité du FemoSeal™ Vascular Closure System (VCS).

Vous trouverez un résumé des performances cliniques et de sécurité du dispositif, destiné aux utilisateurs/professionnels de la santé, à la **Section 1.0**.

## **1.0 RESUME POUR LES UTILISATEURS/PROFESSIONNELS DE LA SANTE**

Ce SSCP n'est pas destiné à remplacer le mode d'emploi, qui est le principal document permettant de garantir une utilisation sûre du dispositif, ni à fournir des suggestions diagnostiques ou thérapeutiques aux utilisateurs auxquels le dispositif est destiné ou aux patients. Ce SSCP n'est pas destiné à remplacer les informations obligatoires figurant sur les cartes d'implant ou dans tout autre document obligatoire.

### **1.1 Utilisation prévue du dispositif**

#### **1.1.1 Utilisation prévue**

Le FemoSeal™ Vascular Closure System est un dispositif médical destiné à la fermeture d'une ponction artérielle après cathétérisme percutané par l'artère fémorale commune.

#### **1.1.2 Indications d'utilisation**

Le FemoSeal™ Vascular Closure System est indiqué pour la fermeture de la ponction artérielle dans l'artère fémorale commune (artériotomie) chez des patients qui ont subi un cathétérisme percutané à l'aide d'une gaine procédurale de 7F (2,33 mm) ou moins.

#### **1.1.3 Contre-indications et/ou limitations**

Le FemoSeal™ Vascular Closure System est contre-indiqué chez les patients qui ont subi une artériotomie où des gaines ou des dispositifs de plus de 2,33 mm (7F) ont été utilisés.

#### **1.1.4 Populations cibles de patients**

La sécurité et l'efficacité du FemoSeal™ Vascular Closure System ont été établies chez les patients âgés de 18 ans et plus qui ont subi un cathétérisme percutané à l'aide d'une gaine procédurale de 2,33 mm (7F) ou moins.

#### **1.1.5 Populations spéciales de patients**

L'innocuité et l'efficacité du FemoSeal™ Vascular Closure System n'ont pas été établies chez les populations de patients suivantes :

- Patients atteints d'une maladie auto-immune préexistante.
- Patients subissant une thrombolyse thérapeutique.
- Patients atteints d'une maladie vasculaire périphérique cliniquement significative.
- Patients souffrant d'hypertension non contrôlée (systolique > 220 mmHg ou diastolique > 110 mmHg).

- Patients présentant des troubles hémorragiques, y compris une thrombocytopénie ( $< 100\,000$  plaquettes) ou une anémie ( $\text{Hgb} < 10 \text{ mg/dl}$ ).
- Patients ayant une lumière interne de l'artère fémorale commune inférieure à 5 mm.
- Patients souffrant d'insuffisance rénale et/ou hépatique.
- Patients présentant d'autres comorbidités pertinentes.
- Population d'une origine raciale et/ou ethnique spécifique.
- Patients ayant présenté un infarctus du myocarde dans les 72 heures.
- Patients ayant une endoprothèse vasculaire ou un stent sur le site de ponction.
- Patientes enceintes ou allaitantes.
- Patients de moins de 18 ans.

### 1.1.6 Utilisateurs auxquels le dispositif est destiné

Les utilisateurs auxquels le FemoSeal™ Vascular Closure System est destiné sont des médecins qui ont suivi une formation leur permettant d'effectuer un accès et une fermeture artériels pour des procédures endovasculaires par le biais de l'artère fémorale commune et qui ont participé à un programme de formation pour médecins FemoSeal™ de Terumo Medical Corporation.

## 1.2 Description du dispositif

### 1.2.1 Description du dispositif

Le FemoSeal™ Vascular Closure System, fabriqué par Terumo Medical Corporation (TMC), est un dispositif de fermeture vasculaire résorbable conçu pour obtenir une hémostase de l'artère fémorale après cathétérisme percutané par l'artère fémorale commune.

Le dispositif de fermeture FemoSeal™ se compose de deux disques en polymère résorbable, le joint interne et le disque externe de verrouillage, qui sont maintenus ensemble par un multifilament résorbable, scellant ainsi mécaniquement l'artériotomie (voir **Schéma 1.1** et **Schéma 1.2**). Après son déploiement dans la gaine du boîtier conique, le disque de verrouillage externe est compacté sur la tige multifilament, ce qui entraîne la fermeture mécanique du site de ponction entre les disques de verrouillage interne et externe. Le disque d'étanchéité intérieur et le disque de verrouillage extérieur sont maintenus en place par friction sur la tige multifilament. L'hémostase est obtenue par des moyens mécaniques. Les éléments de fermeture sont dégradés par hydrolyse.

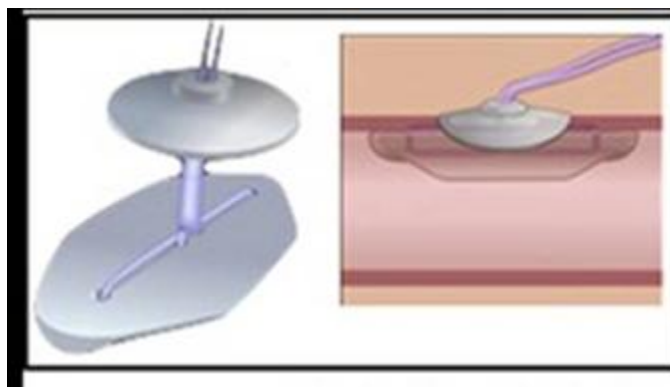
Les composants de fermeture implantables, le joint interne et le disque externe de verrouillage, sont dégradés en dix-huit (18) mois tandis que le multifilament est dégradé et absorbé par

hydrolyse par les tissus environnants après environ deux (2) à trois (3) ans. La capacité des composants de fermeture implantables à maintenir la compression sur l'artériotomie a été testée jusqu'à huit (8) heures. Les produits de dégradation sont métabolisés et excrétés dans l'urine ou expirés sous forme de dioxyde de carbone par les poumons. Aucun effet d'accumulation n'a été observé dans les études animales. Les composants supplémentaires de FemoSeal™ qui entreront en contact avec des tissus vivants ou du sang pendant l'intervention sont la gaine du boîtier conique, le dilateur, la tubulure de protection, le poussoir et le fil-guide.

**Schéma 1.1 Joint intérieur et disque de verrouillage externe, respectivement**

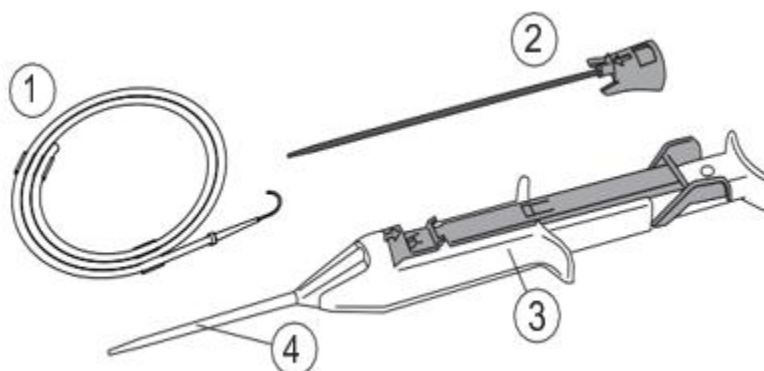


**Schéma 1.2 Joint intérieur et disque de verrouillage externe déployés**



L'unité FemoSeal™ est emballée avec un dilateur et un fil-guide de 0,038" (0,97 mm) de diamètre extérieur, de 27,5" (70 cm) de long et un redresseur en forme de J (voir **Schéma 1.3** ci-dessous). Le fil-guide est contenu dans une tubulure en polyéthylène. Toutes les pièces sont emballées dans un plateau en papier fixe. L'emballage comprend également la carte d'implant du patient. Le FemoSeal™ Vascular Closure System ne nécessite pas d'accessoires supplémentaires pour que le dispositif fonctionne comme prévu et le dispositif est uniquement destiné à être utilisé avec le dilateur et le fil-guide inclus dans le conditionnement du produit.

### Schéma 1.3 Unité FemoSeal™ VCS avec fil-guide et dilateur



#### 1.2.2 Matières premières et composants

Le **Tableau 1.1** ci-dessous répertorie les composants du FemoSeal™ VCS.

**Tableau 1.1 Matières premières et composants du FemoSeal™ VCS**

| N° de référence | Description                                                                     | Matériaux                                                                                                                                                                               |
|-----------------|---------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1               | Fil-guide de 0,038" (0,97 mm) avec un redresseur en forme de J pour fil-guide   | Fil-guide : Acier inoxydable 304<br><br>Redresseur en forme de J : Polypropylène, pigment violet<br><br>Attache : Polyéthylène<br><br>Tubulure : Polyéthylène                           |
| 2               | Dilatateur FemoSeal™                                                            | Embase : Tétrahydrofurane, pigment bleu, polybutylène téréphtalate (PBT)<br><br>Tubulure : Polyéthylène haute densité (PEHD), pigment noir<br><br>Lubrifiant : Silicone Dow Corning 360 |
| 3/4             | Unité FemoSeal™                                                                 |                                                                                                                                                                                         |
|                 | RD7 moulé – Disque d'étanchéité intérieur et disque de verrouillage extérieur * | Copolymère entre le glycolide, le carbonate de triméthylène, l'ε-caprolactone et le triméthylolpropane (TMP) (initiateur)                                                               |
|                 | Multifilament *                                                                 | Copolymère segmenté entre le L,L-lactide, le carbonate de triméthylène, l'ε-caprolactone et le propane-1,3-diol (initiateur)                                                            |



|  |  |                          |                                                                                     |
|--|--|--------------------------|-------------------------------------------------------------------------------------|
|  |  |                          | Le revêtement est un copolymère entre le glycolide, l'ε-caprolactone et la L-lysine |
|  |  | Tubulure de compactage   | Polypropylène                                                                       |
|  |  | Poussoir                 | Acier inoxydable 304V                                                               |
|  |  | Bras                     | Poly(téréphtalate de butylène) (PBT)                                                |
|  |  | Boîtier                  | Poly(téréphtalate de butylène) (PBT)                                                |
|  |  | Bouton                   | Poly(téréphtalate de butylène) (PBT)                                                |
|  |  | Couvercle à bouton       | Copolymère de polyoxyméthylène (POM)/polyacétal                                     |
|  |  | Manchon                  | Poly(téréphtalate de butylène) (PBT)                                                |
|  |  | Espaceur                 | Poly(téréphtalate de butylène) (PBT)                                                |
|  |  | Cône                     | Polypropylène                                                                       |
|  |  | Couvercle du boîtier     | Poly(téréphtalate de butylène) (PBT)                                                |
|  |  | Arrêt de sécurité        | Poly(téréphtalate de butylène) (PBT), pigment bleu                                  |
|  |  | Couvercle du manchon     | Poly(téréphtalate de butylène) (PBT)                                                |
|  |  | Joint de tubulure        | Silicone shore A 70                                                                 |
|  |  | Joint du boîtier         | Silicone shore A 50                                                                 |
|  |  | Ressort                  | Acier inoxydable 302                                                                |
|  |  | Gaine du boîtier conique | Polypropylène<br>Silicone Dow Corning 360, hexane                                   |

\* Partie implantable de l'appareil ; les composants implantables sont compatibles avec l'IRM

Le FemoSeal™ VCS est stérilisé à l'oxyde d'éthylène (OE) et est un dispositif médical à usage unique. Le FemoSeal™ VCS est conçu de manière à ne pas pouvoir être réutilisé.

### **Mode de fonctionnement**

Le FemoSeal™ VCS favorise l'hémostase mécanique en déployant des éléments de fermeture implantables à l'intérieur et à l'extérieur de l'artère fémorale commune. Le joint interne ferme hermétiquement le site de ponction et le disque externe maintient le joint interne en place, empêchant le saignement.

### 1.2.3 Bénéfice clinique

Le FemoSeal™ VCS offre les bénéfices cliniques suivants par rapport à la fermeture vasculaire après une ponction artérielle dans l'artère fémorale commune :

- Réduction du délai avant l'hémostase <sup>1</sup>
- Réduction du délai avant la déambulation <sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

### 1.2.4 Génération(s) précédente(s) ou variantes

- La première version du FemoSeal™ VCS (#11200) a été vendue sur le marché européen au cours de l'année 2005 et de l'année 2006.
- Le FemoSeal™ VCS actuel (#11202), avec un système de distribution amélioré, est sur le marché depuis le 28 mars 2006.

### 1.2.5 Accessoires destinés à être utilisés en combinaison avec le dispositif

L'unité FemoSeal™ est emballée avec un dilateur et un fil-guide de 0,038" (0,97 mm) de diamètre extérieur, de 27,5" (70 cm) de long et un redresseur en forme de J. Le fil-guide est un accessoire de l'unité FemoSeal™. Le redresseur en forme de J est un composant du fil-guide, tandis que le dilateur est un composant de l'unité FemoSeal™. Le fil-guide est le seul accessoire pris en compte. Le fil-guide est contenu dans une tubulure en polyéthylène. Toutes les pièces sont emballées dans un plateau en papier fixe. L'emballage comprend également la carte d'implant du patient. Le FemoSeal™ Vascular Closure System ne nécessite pas d'accessoires supplémentaires pour que le dispositif fonctionne comme prévu et le dispositif est uniquement destiné à être utilisé avec le dilateur et le fil-guide inclus dans le conditionnement du produit.

### 1.2.6 Autres dispositifs et produits destinés à être utilisés en combinaison avec le dispositif

Le FemoSeal™ VCS ne nécessite pas d'appareils supplémentaires pour fonctionner comme prévu.

## 1.3 Risques et avertissements

### 1.3.1 Risques résiduels et effets indésirables

Les effets indésirables, les dommages et les complications connus ou prévisibles liés à l'utilisation du FemoSeal™ VCS en raison d'un risque résiduel sont énumérés dans le **Tableau 1.2**. Le taux d'occurrence se base sur une analyse de la documentation sur les risques et est calculé sur la base des données de surveillance post-commercialisation obtenues du

1<sup>er</sup> septembre 2019 au 31 août 2024. Il n'y a pas de risques résiduels inconnus pour le FemoSeal™ VCS et tous les risques applicables ont été traités par le biais du mode d'emploi et du processus de gestion des risques.

**Tableau 1.2. Événements indésirables/complications du FemoSeal**

| Domage                                                  | Taux de fréquence (%) | Facteurs d'atténuation                                                                                                                                                                                                               |
|---------------------------------------------------------|-----------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Réaction allergique                                     | 0,0000                | Les mesures et les plans visant à réduire les risques au minimum ont été pris en compte dans les caractéristiques de conception des produits, les directives de fabrication, l'étiquetage des produits et la formation des médecins. |
| Anévrisme                                               | 0,0000                |                                                                                                                                                                                                                                      |
| Fistule AV                                              | 0,0001                |                                                                                                                                                                                                                                      |
| Perte de sang/saignement                                | 0,0280                |                                                                                                                                                                                                                                      |
| Décès                                                   | 0,0002                |                                                                                                                                                                                                                                      |
| Ecchymose                                               | 0,0000                |                                                                                                                                                                                                                                      |
| Embolie                                                 | 0,0000                |                                                                                                                                                                                                                                      |
| Réaction au corps étranger                              | 0,0000                |                                                                                                                                                                                                                                      |
| Hématome                                                | 0,0027                |                                                                                                                                                                                                                                      |
| Hémorragie                                              | 0,0001                |                                                                                                                                                                                                                                      |
| Infection                                               | 0,0002                |                                                                                                                                                                                                                                      |
| Réaction inflammatoire                                  | 0,0000                |                                                                                                                                                                                                                                      |
| Engourdissement                                         | 0,0000                |                                                                                                                                                                                                                                      |
| Douleur                                                 | 0,0000                |                                                                                                                                                                                                                                      |
| Inconfort du patient                                    | 0,0004                |                                                                                                                                                                                                                                      |
| Retard de la procédure                                  | 0,0065                |                                                                                                                                                                                                                                      |
| Pseudo-anévrisme                                        | 0,0004                |                                                                                                                                                                                                                                      |
| Saignement rétro-péritonéal                             | 0,0002                |                                                                                                                                                                                                                                      |
| Septicémie                                              | 0,0000                |                                                                                                                                                                                                                                      |
| Thromboembolie                                          | 0,0000                |                                                                                                                                                                                                                                      |
| Thrombose                                               | 0,0001                |                                                                                                                                                                                                                                      |
| Occlusion des vaisseaux/ischémie des membres inférieurs | 0,0002                |                                                                                                                                                                                                                                      |
| Perforation vasculaire                                  | 0,0000                |                                                                                                                                                                                                                                      |
| Dissection/lacération des tissus vasculaires            | 0,0003                |                                                                                                                                                                                                                                      |

### 1.3.2 Avertissements et mises en garde

#### Avertissements

1. Ne pas utiliser si l'emballage a été endommagé ou si une barrière stérile n'est pas intacte.
2. Ne pas utiliser après la date de péremption – les composants biodégradables risquent de ne pas fonctionner correctement.
3. Ne pas utiliser si un élément semble endommagé ou défectueux de quelque manière que ce soit.
4. L'utilisation du FemoSeal™ Vascular Closure System en cas de contamination bactérienne de la gaine procédurale ou des tissus environnants peut provoquer une infection.
5. En cas de suspicion de ponction de la paroi artérielle postérieure ou de plus d'une ponction artérielle, ne pas se fier uniquement au FemoSeal™ Vascular Closure System pour obtenir une hémostase artérielle. Utiliser une compression manuelle ou mécanique supplémentaire.
6. Si le site de ponction se trouve au niveau de la bifurcation de l'artère fémorale ou à proximité de celle-ci, le FemoSeal™ Vascular Closure System ne doit pas être utilisé en raison du risque de mauvais positionnement du joint interne. Cet événement peut entraîner des hémorragies et/ou perturber le débit de sang normal.
7. En cas de saignement artériel persistant au niveau du site d'incision, ne pas couper le multifilament avant d'avoir obtenu l'hémostase. Si l'hémostase n'est pas obtenue, fixer le multifilament à l'aide d'un pansement stérile et appliquer une compression supplémentaire jusqu'à obtention de l'hémostase. En cas d'hémorragie artérielle persistante, des complications hémorragiques importantes peuvent survenir et entraîner des blessures ou le décès du patient.
8. Ne pas utiliser le FemoSeal™ Vascular Closure System si le site de ponction se trouve à proximité du ligament inguinal, car cela pourrait entraîner un hématome rétro-péritonéal.
9. Les patients présentant un risque plus élevé de saignement peuvent subir une perte sanguine accrue, nécessitant une transfusion.
10. Si le disque interne se détache, il peut entraîner un événement thrombotique et/ou embolique.

#### Précautions

1. Le FemoSeal™ Vascular Closure System doit être déployé par des praticiens ayant suivi une formation adéquate sur l'utilisation de l'appareil.

2. Effectuer une angiographie fémorale limitée ou une ponction fémorale guidée par échographie avant de déployer le FemoSeal™ Vascular Closure System.
3. Interrompre la procédure si :
  - le diamètre de la lumière de l'artère fémorale commune < 5 mm,
  - une sténose et/ou une plaque significative sont présentes à proximité du site de ponction de l'artère fémorale commune,
  - la ponction artérielle se situe au niveau de la bifurcation de l'artère fémorale ou à proximité de celle-ci,
  - des branches anormales ou des vaisseaux anormaux se trouvent à proximité du site de ponction de l'artère fémorale commune.
4. En cas d'hématome, une attention particulière doit être portée à l'insertion correcte de la gaine du boîtier conique dans l'artère.
5. Utiliser une méthode de ponction en simple paroi. Ne pas pratiquer de ponction sur la paroi postérieure de l'artère.
6. Toujours respecter une technique stérile lors de l'utilisation du FemoSeal™ Vascular Closure System.
7. Le FemoSeal™ Vascular Closure System est à usage unique et ne doit en aucun cas être réutilisé ou restérilisé. L'unité FemoSeal™ est conçue de manière à ne pas pouvoir être réutilisée.
8. Si le déploiement du joint intérieur rencontre une résistance inattendue, interrompre la procédure.
9. Pour un déploiement correct du joint intérieur, repositionner le pousseur de sorte que le bouton puisse revenir librement en arrière.
10. S'assurer que l'extrémité de la gaine du boîtier conique de l'unité FemoSeal™ se trouve sous la surface de la peau avant de déployer le disque externe de verrouillage. Le disque externe de verrouillage peut être déployé par inadvertance au-dessus du niveau de la peau chez les patients présentant une courte distance entre l'artère fémorale et le niveau de la peau.
11. Pour un déploiement correct, une incision cutanée peut être nécessaire avant le déploiement.
12. Si le joint intérieur se trouve à l'intérieur de l'artère, mais qu'il n'est pas possible d'enfoncer complètement le bouton et de déployer le disque externe de verrouillage, une intervention chirurgicale peut être nécessaire pour retirer les éléments de fermeture FemoSeal™.

13. Si une nouvelle ponction de la même artère fémorale s'avère nécessaire dans les 18 mois, elle doit être effectuée à au moins un centimètre du site d'accès précédent du FemoSeal™ Vascular Closure System.
14. Demander au patient de suivre les instructions du médecin concernant l'inspection du site de fermeture.
15. Demander au patient de porter la carte d'information du patient pendant les 18 prochains mois

### **Précautions au moment de la sortie**

Avant d'envisager la sortie, évaluer l'état du patient en ce qui concerne les conditions cliniques suivantes :

1. Saignement et/ou hématome au niveau du site de fermeture.
2. Douleur à la marche.
3. Signes d'infection au niveau du site de fermeture.

### **1.3.3 Mesures correctives de sécurité sur le terrain**

Une mesure corrective de sécurité a été prise sur le terrain concernant le FemoSeal™ VCS entre le 1<sup>er</sup> septembre 2019 et le 31 août 2024.

En 2022, Terumo a volontairement rappelé le FemoSeal™ VCS en raison de plaintes alléguant des échecs lors des tests des processus et de commercialisation de lots de produits FemoSeal fabriqués par Elkton pour la mesure de la force de compression et de la force de rétraction. Au total, 950 unités ont été rappelées en Corée du Sud.

## **1.4 Évaluation clinique et suivi clinique post-commercialisation**

Le **Tableau 1.3** comprend une liste d'études pivots incluses pour mettre le FemoSeal™ VCS sur le marché ainsi que des études post-commercialisation et des activités de suivi clinique post-commercialisation. La version de l'appareil utilisée dans l'étude est incluse dans le tableau ci-dessous. La première version du FemoSeal™ VCS (#11200) a été commercialisée jusqu'en 2006, tandis que la version suivante (#C11202) a été mise sur le marché en 2006 et est toujours commercialisée à l'heure actuelle.

**Tableau 1.3 Résumé des études pivots**

| <b>Essais fonctionnels pré-commercialisation sur des animaux</b>                                                                                                                                                                                                        | <b>Version du dispositif</b> |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                        |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                        |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                        |
| <b>Première étude clinique chez l'homme</b>                                                                                                                                                                                                                             |                              |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                        |
| <b>Études cliniques post-commercialisation terminées</b>                                                                                                                                                                                                                |                              |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                                                                              | C11202<br>(appareil actuel)  |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                                                                                       | C11202<br>(appareil actuel)  |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                                                                                                                                                          | C11202<br>(appareil actuel)  |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)                                                                                                                                                  | C11202<br>(appareil actuel)  |
| <b>Études cliniques post-commercialisation planifiées/en cours</b>                                                                                                                                                                                                      |                              |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                                                                                                                                                              | C11202<br>(appareil actuel)  |
| <b>Activités de suivi clinique post-commercialisation</b>                                                                                                                                                                                                               |                              |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                                                                                                                                                               | C11202<br>(appareil actuel)  |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                                                                                                                                                                      | C11202<br>(appareil actuel)  |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024)                                                                                                                                         | C11202<br>(appareil actuel)  |

### 1.4.1 Résumé des données des études avant la mise sur le marché (animales et cliniques)

Le **Tableau 1.4** ci-dessous décrit toutes les études avant la mise sur le marché, tant animales que cliniques.

**Tableau 1.4 Résumé des études avant la mise sur le marché**

| Essais fonctionnels pré-commercialisation sur des animaux                                                                                                                                                                                                               |                                                                      |                                         |                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------|-----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Nom de l'étude                                                                                                                                                                                                                                                          | Année/CI                                                             | Type d'étude                            | Objectifs                                                                                                                                                                                                                                                        | Étapes clés                                                                                                                                                                                                                                                                                                                                                       | Critères d'acceptation potentielle                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 2 000<br>Radi Medical System AB<br><br>Réalisé par Biomatech, France | Étude animale ;<br>Enquête exploratoire | L'objectif de l'étude était d'évaluer la biocompatibilité et la biofonctionnalité d'un implant biodégradable conçu pour atteindre l'hémostase dans le système vasculaire. Le rapport concerne les animaux de réserve du numéro d'étude 862 (document n° 1051-01) | N = 3 moutons femelles adultes, 1 animal par point temporel<br><br>Suivi pour l'analyse histopathologique, le classement macroscopique et l'analyse ultrastructurale<br><br><ul style="list-style-type: none"> <li>12 mois</li> <li>15 mois</li> <li>18 mois</li> </ul><br>Suivi écho-Doppler couleur – 30 jours aux sites d'accès artériel carotidien et fémoral | Perméabilité artérielle <ul style="list-style-type: none"> <li>Évaluation du débit de sang post-déploiement – 2/3 de la diminution du débit de sang associée à un spasme artériel temporaire qui a été attribué à l'intervention, tous deux survenant au niveau de l'artère carotide commune gauche</li> <li>Évaluation écho-Doppler couleur (4 semaines) - 3/3 (100 %) sans diminution majeure du débit de sang 30 jours après l'implantation</li> </ul><br>Observations macroscopiques <ul style="list-style-type: none"> <li>12 mois – perméabilité confirmée macroscopiquement par l'absence d'occlusion anatomiquement visible ; aucune lésion macroscopique d'intolérance locale (hémorragie, nécrose ou néovascularisation) ; l'encapsulation du disque interne semblait marquée</li> <li>15 mois – l'observation macroscopique n'a montré aucun signe d'inflammation ; aucun résidu de disques internes ou externes n'a été identifié ; le tissu d'encapsulation situé dans la zone du disque externe est apparu identique à celui de l'observation à 12 mois</li> <li>18 mois – l'observation macroscopique n'a montré aucun signe d'intolérance locale, disque externe visible</li> </ul> |



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|                                                                                                                                                                                                                                                                                |                                                                         |                                             |                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                         | <p>(3/3 cas), dégradation du disque interne terminée ;<br/>1/3 (artère carotide commune gauche) - dépression de la paroi artérielle observée au niveau du site d'implantation (peut être liée au déploiement de l'appareil)</p> <p>Conclusions</p> <ul style="list-style-type: none"> <li>• Au niveau macroscopique, 12, 15 et 18 mois après l'implantation, aucun signe nécrotique, dégénératif ou thrombotique n'a été observé.</li> <li>• Le processus de dégradation des disques interne et externe a semblé progresser entre 12 et 18 mois et s'est terminé à 18 mois, un tissu blanchâtre recouvrant la zone de l'implantation.</li> <li>• Sur le plan histologique, après 18 mois, le matériau polymère n'était plus visible, mais un tissu fibreux endoluminal était présent. Aucune lésion nécrotique, dégénérative ou thrombotique n'a été observée.</li> </ul> |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002 Radi Medical System AB</p> <p>Réalisé par Biomatech, France</p> | <p>Étude animale ; Enquête exploratoire</p> | <p>L'objectif de l'étude était d'évaluer la biocompatibilité d'un implant biodégradable conçu pour atteindre l'hémostase dans le système vasculaire.</p> | <p>Suivi (après l'implantation)</p> <ul style="list-style-type: none"> <li>• 12 semaines</li> <li>• 24 semaines</li> <li>• 36 semaines</li> </ul> <p>N = 12 moutons, 3 animaux par point temporel, 3 animaux de réserve sacrifiés à 12, 15 et 18 mois</p> <p>Sites d'implantation – artères fémorales droite et gauche, artères carotides communes droite et gauche</p> | <p><u>Perméabilité des artères carotides et fémorales après 4 semaines</u></p> <ul style="list-style-type: none"> <li>• Diminution importante du débit de sang 0/12 (0 %)</li> </ul> <p><u>Pas de diminution majeure du débit de sang</u></p> <ul style="list-style-type: none"> <li>• Insuffisance grave du débit de sang liée à la pose de l'appareil 0/12 (0 %)</li> <li>• Diminution du débit de sang dans la carotide commune gauche 2/12 (16,6 %) en raison d'un spasme artériel temporaire (attribué à l'intervention)</li> </ul>                                                                                                                                                                                                                                                                                                                                  |

|  |  |  |  | Analyse par écho-Doppler couleur | <p>chirurgicale, pas à l'appareil)</p> <p><u>Altération du débit de sang par suivi</u></p> <p>12 semaines – 0/12 (0 %)</p> <p>24 semaines – 0/12 (0 %)</p> <p>36 semaines – 0/12 (0 %)</p> <p>Mesure de la pression artérielle (3 moutons – 36 semaines)</p> <ul style="list-style-type: none"> <li>Pas de diminution majeure du débit de sang observée</li> </ul> <p>Données macroscopiques pour l'intégration et la dégradation (niveau 0 - 4)</p> <p><u>Sites carotidiens</u></p> <p><u>Largeur interne</u></p> <p>- encapsulation</p> <p>12 semaines 1,3</p> <p>24 semaines 0,8</p> <p>36 semaines 0,7</p> <p>- dégradation des matériaux</p> <p>12 semaines 2,2</p> <p>24 semaines 2,3</p> <p>36 semaines 0,7</p> <p><u>Côté extérieur</u></p> <p>- encapsulation</p> <p>12 semaines 2,0</p> <p>24 semaines 1,0</p> <p>36 semaines 0,8</p> <p>- dégradation des matériaux</p> <p>12 semaines 2,0</p> <p>24 semaines 2,7</p> <p>36 semaines 3,2</p> <p><u>Sites fémoraux</u></p> <p><u>Côté extérieur</u></p> <p>- encapsulation</p> <p>12 semaines 1,0</p> <p>24 semaines 2,7</p> <p>36 semaines 1,0</p> <p>- dégradation des matériaux</p> <p>12 semaines 2,0</p> <p>24 semaines 2,4</p> <p>36 semaines 3,0</p> |
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|  |  |  |  |  | <p><i>Largeur interne</i></p> <p>- encapsulation</p> <p>12 semaines 2,0</p> <p>24 semaines 1,2</p> <p>36 semaines 1,0</p> <p>- dégradation des matériaux</p> <p>12 semaines 1,0</p> <p>24 semaines 2,2</p> <p>36 semaines 3,0</p> <p><u>Données histologiques pour les paramètres d'intégration, de dégradation et d'inflammation (moyenne des valeurs pertinentes, Indice 0 - 4) n = 6</u></p> <p><u>Sites carotidiens</u></p> <p>Fibrose externe</p> <p>12 semaines – 2,3</p> <p>24 semaines – 2,3</p> <p>36 semaines – 1,8</p> <p>Néo-intima interne</p> <p>12 semaines – 3,0</p> <p>24 semaines – 2,7</p> <p>36 semaines – 3,3</p> <p>Dégradation du matériau</p> <p>12 semaines – 1,7</p> <p>24 semaines – 3,0</p> <p>36 semaines – 3 +</p> <p>Paramètres inflammatoires (macrophages)</p> <p>12 semaines – 3,0</p> <p>24 semaines – 1,7</p> <p>36 semaines – 1,7</p> <p><u>Sites fémoraux</u></p> <p>Fibrose externe</p> <p>12 semaines – 1,3</p> <p>24 semaines – 1,5</p> <p>36 semaines – 1,7</p> <p>Néo-intima interne</p> <p>12 semaines – 3,7</p> <p>24 semaines – 3,3</p> <p>36 semaines – 3,8</p> <p>Dégradation du matériau</p> <p>12 semaines – 2,0</p> <p>24 semaines – 3,0</p> <p>36 semaines – 3 +</p> <p>Paramètres inflammatoires (macrophages)</p> <p>12 semaines – 3,5</p> |
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|                                                                                                                                                                                                                    |                                                                                |                              |                                                                                                                                                                                                                                                          |                                                                                                                                            | <p>24 semaines – 1,8<br/>36 semaines – 1,8</p> <p><u>Valeurs de perméabilité histomorphologique</u></p> <p>Sites carotidiens<br/>12 semaines - 74 %<br/>24 semaines - 81,9 %<br/>36 semaines - 89,43 %</p> <p>Sites fémoraux<br/>12 semaines – 42,2 %<br/>24 semaines – 73,21 %<br/>36 semaines – 78,71 %</p> <p><u>Perméabilité des vaisseaux aux États-Unis (% moyen)</u></p> <p>Site carotidien<br/>12 semaines - 94,6 %<br/>24 semaines – 96,7 %<br/>36 semaines – 94,7 %</p> <p>Sites fémoraux<br/>12 semaines – 66,9 %<br/>24 semaines – 63,6 %<br/>36 semaines – 75,1 %</p> <p>Conclusions</p> <ul style="list-style-type: none"> <li>Aucun signe d'intolérance locale significative n'a été détecté (absence de lésions inflammatoires, nécrotiques ou dégénératives visibles) à 12, 24 ou 36 semaines</li> <li>Aucune réaction tissulaire indésirable significative n'a été notée concernant l'hôte et l'appareil</li> <li>La dégradation de l'implant était presque terminée à 36 semaines.</li> </ul> |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi</p> | <p>2002</p> <p>Radi Medical System AB</p> <p>Réalisé par Biomatech, France</p> | <p>Étude sur des animaux</p> | <p>L'objectif de l'étude était d'évaluer la biocompatibilité et la biofonctionnalité d'un implant biodégradable conçu pour atteindre l'hémostase dans le système vasculaire. L'appareil testé était destiné à pénétrer dans l'orifice de la ponction</p> | <p>La période d'implantation/de suivi est de 5 semaines pour tous les animaux</p> <p>4 moutons, 1 porc</p> <p>14 éléments de fermeture</p> | <p>Tous les critères d'effets indésirables (inflammation, nécrose, hémorragie ou toute autre lésion) ou toute formation d'une fine couche pseudo-intimale ont été enregistrés. Une attention particulière a été accordée à l'intégration tissulaire initiale du dispositif, en</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |

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| Medical System AB<br>(performed by<br>Biomatech, France). |  |  | artérielle pour obtenir l'hémostase. Un des disques a pénétré dans l'orifice de ponction et l'autre a serré le disque interne depuis l'extérieur de l'artère. Les deux disques ont été insérés par le biais d'un introducteur. Les disques ont été conçus pour empêcher les saignements, guérir dans la paroi vasculaire et finalement se dégrader et être absorbés. L'étude a été conçue pour recueillir et analyser des données après l'implantation fonctionnelle chez le mouton et le porc afin d'évaluer la capacité de l'implant à maintenir la fonction physiologique lorsqu'il est utilisé dans le système circulatoire, de déterminer la réaction de l'hôte et du dispositif (intégrité physique, encapsulation tissulaire au sacrifice) et d'évaluer la dégradation de l'implant. | 8 éléments de fermeture implantés chez 2 moutons<br><br>2 éléments de fermeture implantés chez 1 porc<br><br>Lorsque deux éléments de fermeture ont été implantés dans la même artère fémorale, ils ont été implantés à une distance > 30 mm | mettant particulièrement l'accent sur l'encapsulation du disque interne.<br><br>Sur le plan macroscopique, aucun signe significatif d'intolérance locale ou de formation de thrombus n'a été observé. L'observation macroscopique n'a pas mis en évidence de différence entre les moutons et le porc après implantation des éléments de fermeture dans les artères fémorales. Sur le plan macroscopique, aucun signe significatif d'intolérance locale ou de formation de thrombus n'a été observé. L'observation macroscopique n'a pas mis en évidence de différence entre les moutons et le porc après implantation des éléments de fermeture dans les artères fémorales.<br><br>L'analyse histopatologique du site d'implantation chez le mouton n'a montré aucun effet indésirable local. Les disques intérieur et extérieur présentaient des signes de dégradation et, dans certains cas, étaient cassés en plus petites parties. Les disques internes ont été complètement intégrés dans le tissu néo-intimal. Chez le porc, l'analyse histopatologique a montré un peu plus de signes inflammatoires autour des disques interne et externe. Chez les deux animaux, le multifilament présentait un peu plus de signes d'inflammation que dans |
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| <b>Première étude clinique chez l'homme</b>                                                                                                                                                                  |                              |                                           |                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| <b>Nom de l'étude</b>                                                                                                                                                                                        | <b>Année/CI</b>              | <b>Type d'étude</b>                       | <b>Objectifs</b>                                                                                                                                                                                                                                                                                                                                           | <b>Étapes clés</b>                                                                                                                                                                                                                                                                                                                                                                        | <b>Critères d'acceptation potentielle</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Essai ouvert, à un groupe, multicentrique | Les objectifs de l'étude étaient de déterminer la sécurité, les performances et l'efficacité du FemoSeal Vascular Closure System (système FemoSeal) en général et, en particulier, des éléments de fermeture chez les patients subissant des procédures de cardiologie diagnostique ou des interventions en cardiologie avec un accès à l'artère fémorale. | <p>Étude en 2 parties</p> <p>Total n = 80</p> <p>Partie 1 n = 20</p> <p>Partie 2 n = 60</p> <p>Indications :</p> <p>Partie 1 – cathétérisme cardiaque diagnostique utilisant l'artère fémorale comme site d'accès</p> <p>Partie 2 – patients subissant des procédures de cardiologie diagnostiques et des interventions de cardiologie utilisant l'artère fémorale comme site d'accès</p> | <p>Résultats</p> <p>- <u>hémostase obtenue avec FS sans compression</u></p> <p>- Partie 1 20/20 (100 %)</p> <p>- Partie 2 58/60 (97 %)</p> <p>Délai médian jusqu'à l'hémostase au moment de l'intervention (partie 2) - 1,0 minute (plage immédiate – 8 minutes)</p> <p><u>Délai avant déambulation (minutes)</u></p> <p>Partie 1 -</p> <p>Moyenne : 33,0</p> <p>Moyenne : 67,8</p>                                                                                                                                                                                                                                                           |

|  |  |  |  | Suivi après 30 jours | Partie°2 -<br>Moyenne : 45<br>Moyenne : 87,5<br><br><u>Incidence des complications vasculaires majeures – suivi à 30 jours</u><br>Partie°1<br>- Sans complications vasculaires 20/20 (100 %)<br>Partie°2<br>Pseudo-anévrisme – 1/59 (1,69 %)<br><br><u>Échec du traitement</u><br>Partie 1 – 0/20 (0 %)<br>Partie 2 – 3/60 (5 %) <ul style="list-style-type: none"> <li>2 en raison de l'absence d'hémostase sans recours à la compression</li> <li>1 en raison d'une complication vasculaire majeure, pseudo-anévrisme</li> </ul><br><u>Suintement persistant</u><br>Partie 1 – 0/20 (0 %)<br>Partie 2 - 8/60 (13 %)<br><br><u>Hématome</u><br>Partie 1 – 0/20 (0 %)<br>Partie 2 – 6/60 (10 %) |
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Dans le cadre du plan de développement avant commercialisation du FemoSeal™ VCS, trois tests fonctionnels ont été réalisés sur des animaux. En 2000, avant de commencer les études cliniques, une étude sur des animaux a été réalisée pour évaluer la biofonctionnalité du FemoSeal™ VCS. Cette étude a évalué la capacité des éléments de fermeture à maintenir la fonction physiologique et à évaluer leur dégradation. À 18 mois, les disques interne et externe n'étaient plus visibles, après avoir été remplacés par un tissu fibreux endoluminal.

En conclusion, la capacité de l'élément de fermeture du FemoSeal™ VCS à maintenir la fonction physiologique lorsqu'il est utilisé dans le système circulatoire a été confirmée.

En 2002, une étude sur des animaux a été réalisée pour évaluer la biocompatibilité et la biofonctionnalité d'un implant biodégradable, le FemoSeal™ VCS, conçu pour atteindre l'hémostase dans le système vasculaire. En résumé, la dégradation de l'implant était presque terminée après 36 semaines et il n'y avait pas de réaction tissulaire indésirable significative.

Une autre étude sur des animaux, réalisée en 2002, a évalué la biocompatibilité et la biofonctionnalité d'un implant biodégradable, le FemoSeal™ VCS, conçu pour obtenir l'hémostase dans le système vasculaire. Après 5 semaines, l'encapsulation du disque était terminée et des signes de dégradation ont été observés pour les disques internes et externes. En conclusion, la capacité de l'implant à maintenir la fonction physiologique lorsqu'il est utilisé dans le système circulatoire a été confirmée.

Dans le cadre du plan de développement clinique du FemoSeal™ VCS, Radi Medical System AB a mené une étude clinique avant la mise sur le marché. Cette étude clinique n'a pas été publiée et n'est pas disponible en ligne. L'étude portant sur le modèle #11200 a été menée entre 2002 et 2004 dans le cadre de la norme européenne EN 540 (Investigation clinique des dispositifs médicaux sur les sujets humains) et conformément aux Considérations générales de l'ICH relatives aux essais cliniques et aux directives de bonnes pratiques cliniques. Les détails de cette étude sont documentés dans le rapport EU-SE-001. L'étude clinique a été documentée dans le rapport final de Radi Medical Systems AB, « Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures ». L'étude clinique a été réalisée avec le premier modèle #11200 de FemoSeal et s'est concentrée sur la sécurité et l'efficacité des composants de fermeture implantables. La seule différence entre le premier modèle #11200 et le modèle actuel, C11202, est la taille française, respectivement 6F et 7F, et l'amélioration du système de distribution. Les bénéfices cliniques, l'utilisation prévue, le mode de fonctionnement et les matières premières des éléments de fermeture implantables, du joint interne et du disque externe de verrouillage restent inchangés.

L'appareil a été conçu pour être utilisé comme point d'accès dans l'artère fémorale chez des patients qui subissent un examen cardiaque de diagnostic ou une intervention cardiaque. L'objectif de cette étude était de déterminer la sécurité, les performances et l'efficacité du FemoSeal™ VCS. Il s'agissait d'une étude ouverte, prospective, multicentrique, à un groupe avec un suivi à 30 jours.

Le critère d'évaluation principal de la performance était le délai avant l'hémostase, défini comme l'absence de saignements rapides. Le critère d'évaluation principal de l'innocuité était l'incidence des complications vasculaires majeures pendant 30 jours. Les critères d'évaluation secondaires comprenaient le délai avant la déambulation, la proportion d'échecs du traitement,



la fréquence des événements indésirables et les caractéristiques de performance de l'appareil pendant l'administration et le déploiement.

Les patients inclus dans cette étude étaient des adultes capables de fournir un consentement éclairé et ayant au moins un pouls pédieux intact. Les patients ont été exclus de l'étude s'ils présentaient l'une des pathologies suivantes :

- Antécédents de maladie vasculaire périphérique
- Maladie auto-immune
- Trouble hémorragique connu de l'anémie sévère
- INR > 1,5
- Infarctus du myocarde dans les 72 heures
- Hypertension non contrôlée malgré le traitement
- Obésité empêchant l'accès avec la technique de Seldinger
- Présence d'une endoprothèse vasculaire ou d'un stent au niveau du site de l'artériotomie
- Ponction ipsilatérale précédente dans les 3 mois
- Espérance de vie < 6 mois

En outre, les patients ont été examinés en peropératoire et exclus de l'étude si l'une des conditions suivantes était observée :

- Diamètre de la lumière de l'artère fémorale commune < 5 mm
- Branches artérielles à moins de 2 cm du site de ponction
- Sténose significative à 3 cm du site de ponction
- Utilisation d'un introducteur principal > 6 Fr
- Ponction au niveau de la bifurcation fémorale ou à proximité de celle-ci
- Ponctions fémorales multiples
- Ponction connue ou suspectée de la paroi fémorale postérieure
- Hématome important (2:6 cm) à la fin de la procédure
- Insertion difficile de l'introducteur principal pour l'intervention en raison d'un tissu ou d'un vaisseau tortueux

Cette étude à protocole unique a été menée en deux parties : 20 patients ont été recrutés pendant la Partie 1, puis une analyse de l'innocuité a été réalisée et 60 patients supplémentaires ont été recrutés pendant la Partie 2.

Dans la partie 1, l'âge moyen des patients recrutés était de 65,9 ans, 70 % des patients étaient des hommes et 95 % des patients avaient un traitement concomitant. Dans la partie 2 de l'étude, l'âge moyen était de 63,8 ans, 78 % étaient des hommes et 100 % avaient un traitement concomitant.

Les patients subissant des procédures de cathétérisme cardiaque diagnostique (Partie 1 et Partie 2) ou interventionnel (Partie 2) étaient éligibles pour participer à l'étude. Les procédures étaient conformes aux normes de soins dans chacun des hôpitaux participants, suivies de l'utilisation du FemoSeal™ VCS. Les données des patients ont été recueillies à l'entrée dans l'étude, pendant la procédure et 1 jour puis 30 jours après la procédure. Les résultats sont résumés dans le **Tableau 1.5** et indiquent que le FemoSeal™ VCS est sûr et efficace pour cette population de patients.

**Tableau 1.5 Résultats cliniques rapportés lors de l'étude pré-commercialisation**

|                                                                                                                               | Partie <sup>o</sup> 1 | Partie <sup>o</sup> 2     |
|-------------------------------------------------------------------------------------------------------------------------------|-----------------------|---------------------------|
| Nombre de patients                                                                                                            | 20                    | 60                        |
| Temps moyen avant l'hémostase                                                                                                 | 1,2 minute            | 1,6 minute <sup>a</sup>   |
| Temps moyen avant la déambulation                                                                                             | 72,2 minutes          | 87,5 minutes <sup>b</sup> |
| Incidence des complications vasculaires majeures <sup>c</sup>                                                                 | 0 (0 %)               | 1 (2 %)                   |
| Nombre de patients présentant des événements indésirables                                                                     | 5 (25 %)              | 19 (32 %)                 |
| Échec du traitement (défini par des complications vasculaires majeures, la nécessité d'une compression manuelle, ou les deux) | 0 (0 %)               | 3 (5 %)                   |
| Dysfonctionnements de l'appareil                                                                                              | 0 (0 %)               | 6 (10 %)                  |

<sup>a</sup> Sur la base d'un échantillon total de 58 patients, car 2 patients n'ont pas atteint l'hémostase au moment de l'intervention en raison de ponctions ipsilatérales antérieures. L'hémostase a été obtenue à 7 minutes et 37 minutes pour ces patients.

<sup>b</sup> Sur la base d'un échantillon total de 59 patients : 1 patient n'a pas été inclus, car il a été placé sous respirateur en raison d'un œdème pulmonaire et a été incapable de se déplacer pendant plus d'une semaine.

<sup>c</sup> Définie comme une complication vasculaire nécessitant une transfusion sanguine ou une intervention chirurgicale, une infection locale nécessitant l'administration d'une antibiothérapie, une hospitalisation ou une prolongation de l'hospitalisation ou un débridement du site

Aucune complication vasculaire majeure n'a été observée dans la Partie 1 de l'étude. Une complication vasculaire majeure a été signalée dans la Partie 2 de l'étude : un pseudo-anévrisme qui a été signalé un jour après la procédure. L'événement a nécessité une compression guidée par échographie et une injection de thrombine dans le pseudoanévrisme et a prolongé l'hospitalisation du patient.

Sur les cinq événements indésirables signalés dans la Partie 1 de l'étude, il y a eu un événement indésirable possible lié au dispositif : un événement non grave de saignement rapide 1 jour après la procédure. Sur les 19 événements indésirables rapportés dans la Partie 2 de l'étude, trois événements indésirables non graves d'hématome lié au dispositif ont été observés et six événements non graves potentiellement liés au dispositif ont été observés, notamment trois rapports de suintement persistant, deux hématomes et une douleur à la jambe après l'exercice.

Trois patients ont été considérés comme des échecs thérapeutiques dans la Partie 2 : Deux en raison de l'absence d'hémostase sans recours à la compression et un en raison de la complication vasculaire majeure (pseudoanévrisme). Il n'y a pas eu d'échec thérapeutique dans la Partie 1 de l'étude.

Sur les six dysfonctionnements de l'appareil dans la Partie 2 de l'étude, trois n'ont pas interféré avec l'intervention, un a été attribué à une erreur de l'utilisateur, un a fui de l'introducteur et l'autre était une rupture de l'articulation du filament. Les deux derniers problèmes ont été traités avec des mises à jour de modèles mises en œuvre dans C11202.

La Partie 2 de l'étude clinique pré-commercialisation n'a pas rapporté les résultats de suivi à 6 mois en raison de la non-observance du patient. L'étude clinique pré-commercialisation (EU-SE-001) à 30 jours, ce qui est conforme à la période de suivi de la littérature clinique, démontre que le FemoSeal™ VCS est sûr et efficace.

#### 1.4.2 Résumé des données issues des études cliniques post-commercialisation

Quatre études cliniques post-commercialisation ont été menées à bien et sont décrites dans le **Tableau 1.6** ci-dessous. Ces études cliniques n'ont pas été publiées et ne sont pas disponibles en ligne.

**Tableau 1.6 Études cliniques post-commercialisation terminées**

| Études cliniques post-commercialisation terminées                                           |              |                                                        |                                                                                                                                    |                                                                                                                                                         |                                                                                                         |
|---------------------------------------------------------------------------------------------|--------------|--------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|
| Nom de l'étude                                                                              | Année/CI     | Type d'étude                                           | Objectifs                                                                                                                          | Étapes clés                                                                                                                                             | Critères d'acceptation potentielle                                                                      |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI | Post Market Study, User Acceptability of New Packaging | Étude post-commercialisation menée sur l'actualisation du modèle FemoSeal Vascular® Closure System #11202, qui présente un système | 100 patients <ul style="list-style-type: none"> <li>63 hommes/37 femmes</li> <li>Âge moyen de 68 ans pour les femmes, 65 ans pour les hommes</li> </ul> | Résultats<br>1. Illustrations/instructions du mode d'emploi considérées comme informatives et adéquates |

|                                                                                          |                                                                    |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
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|                                                                                          |                                                                    |                                                          | <p>d'administration modifié par rapport au premier modèle, le #11200, pour documenter sa fonctionnalité.</p> <p>L'objectif de l'étude était d'obtenir des commentaires sur le mode d'emploi révisé, le projet de formation pour les médecins et les infirmières, de confirmer les évaluations effectuées dans l'analyse des risques et de donner des informations sur toutes les améliorations de la qualité du produit.</p> | <p>2 hôpitaux suédois, 6 médecins</p> <p>112 dispositifs</p> <p>Données consignées dans les formulaires de dossier patient (CRF)</p> <p>Temps d'observation prévu – 30 minutes à compter de l'application</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | <p>2. Hémostase immédiate (91/100)</p> |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| <p>Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)</p> | <p>Dr. Nicolas Moes<br/>Innsbruck Medical University, Autriche</p> | <p>Évaluation de confirmation post-commercialisation</p> | <p>L'objectif de cette étude était d'évaluer la sécurité et les performances du dispositif FemoSeal® utilisé pendant la routine clinique normale chez des patients subissant un cathétérisme cardiaque diagnostique ou une intervention cardiaque percutanée réalisée avec un introducteur 7F.</p>                                                                                                                           | <p>50 patients consécutifs</p> <p>Indication – cathétérisme cardiaque diagnostique ou invasif à partir de l'artère fémorale commune</p> <table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.6±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                      | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.6±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | <p>Principaux critères d'évaluation</p> <ul style="list-style-type: none"><li>Principal critère d'évaluation de l'efficacité – THT (délai avant l'hémostase) avec ou sans suintement, mais sans compression supplémentaire (manuelle ou mécanique).</li><li>Critère d'évaluation de la sécurité – incidence des événements indésirables – complications vasculaires mineures et majeures et tous les autres événements indésirables – graves et non graves pendant la durée de l'étude (c'est-à-dire jusqu'à la sortie du patient).</li></ul> <p>Résultats</p> <ul style="list-style-type: none"><li>Délai moyen avant l'hémostase</li><li>Diagnostic – 56,6 ± 29 secondes</li><li>Intervention 59,9 ± 16,2 secondes</li><li>Tous les patients 57,8 ± 26,3</li><li>Tous les patients ont pu être mobilisés sans problème après 4 heures de repos au lit.</li></ul> <p>Résultats de sécurité</p> <ul style="list-style-type: none"><li>49/50 (98 %) sans complications vasculaires jusqu'à la sortie de l'hôpital</li></ul> |
| n                                                                                        | 50                                                                 |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| men                                                                                      | 35 (70%)                                                           |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| women                                                                                    | 15 (30%)                                                           |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| PCI cases                                                                                | 15                                                                 |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| age (yrs)                                                                                | 62.6±11.1                                                          |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| body mass index (kg/m²)                                                                  | 25.4±6.7                                                           |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| systolic BP (mmHg)                                                                       | 131.2±20.9                                                         |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| diastolic BP (mmHg)                                                                      | 77.9±10.6                                                          |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| diabetes mellitus                                                                        | 9 (18%)                                                            |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| arterial hypertension                                                                    | 34 (68%)                                                           |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| previous coronary intervention                                                           | 13 (26%)                                                           |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| preprocedure aspirin                                                                     | 50 (100%)                                                          |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| preprocedure clopidogrel                                                                 | 50 (100%)                                                          |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Procedural unfractionated heparin                                                        | 15 (30%)                                                           |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Procedural abciximab                                                                     | 2 (4%)                                                             |                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |

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|                                                                                                                                 |                                 |                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                  | <ul style="list-style-type: none"> <li>Délai moyen avant la sortie de l'hôpital 2,6 jours</li> <li>1/50 (2 %) saignement mineur le lendemain après déambulation sans événement le jour de l'angiographie</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | 2009 RADI                       | Étude post-commercialisation                                         | <p>L'étude doit indiquer si les clients/utilisateurs ont perçu des problèmes avec le nouvel emballage, en particulier le côté externe non stérile de la poche en Tuvek/PET-PE.</p> <p>L'étude doit également indiquer si le médecin traitant perçoit des différences dans les étapes d'application/déploiement du dispositif par rapport aux dispositifs utilisés précédemment.</p> <p>L'étude doit également fournir des informations sur tout autre besoin d'amélioration de la qualité du produit.</p> | <p>25 dispositifs</p> <p>4 hôpitaux suédois</p> <p>16 patients sur 25 (64 %) étaient des patients atteints d'ICP avec des médicaments anticoagulants puissants</p>                                                                                                                                                                                                                                                               | <p>Résultats</p> <ol style="list-style-type: none"> <li>Problèmes liés à l'emballage – 21/25 (84 %) applications ont été menées avec succès ; 4/25 (16 %) ont échoué (1 – test du nouvel introducteur, 1 disque interne a traversé l'artériotomie lors de l'étape d'appui, le bouton est apparu et le disque externe a été placé dans le canal tissulaire de l'incision, 2 l'hémostase n'a pas été obtenue immédiatement malgré l'absence de problème de déploiement).</li> <li>Hémostase immédiate 19/25 (76 %) patients</li> <li>Saignement 11/25 (44 %) - 9/25 (36 %) suintement/saignement, 2/25 (8 %) hématomes</li> </ol> <p>Taux total d'événements 19 %</p> |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022) | 2022/Terumo Medical Corporation | Observationnelle prospective, multicentrique, post-commercialisation | Démontrer davantage l'innocuité et l'efficacité du FemoSeal™ VCS dans l'obtention de l'hémostase du site d'accès par l'artère fémorale commune (AFC) chez des sujets authentiques subissant des procédures endovasculaires percutanées.                                                                                                                                                                                                                                                                   | <ul style="list-style-type: none"> <li>Suivi du patient à 30 jours (<math>\pm</math> 7 jours) avec visite à l'hôpital ou appel téléphonique.</li> <li>Recrutement : décembre 2021 à juillet 2022.</li> <li>Le recrutement de 230 sujets subissant des procédures endovasculaires diagnostiques ou thérapeutiques pour lesquelles le FemoSeal™ est utilisé.</li> </ul> <p>3 sites européens : France (92 patients), Allemagne</p> | <ul style="list-style-type: none"> <li><b>Démographie/comorbidités :</b> <ul style="list-style-type: none"> <li>- Sexe : 161 hommes (70 %)/69 femmes (30 %).</li> <li>- Âge moyen : <math>70 \pm 12</math>.</li> <li>- IMC : <math>26,1 \pm 4,95</math> kg/m<sup>2</sup>.</li> <li>- Hypertension : 160 patients (69,6 %).</li> <li>- Dyslipidémie : 128 (55,7 %).</li> <li>- Maladie coronarienne : 42 (18,3 %).</li> <li>- Fumeur actuel : 86 (37,6 %).</li> <li>- Ex-fumeur : 66 (28,8 %).</li> </ul> </li> </ul>                                                                                                                                                |

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|  |  |  |  | <p>(38 patients), Belgique<br/>(100 patients).</p> | <ul style="list-style-type: none"> <li>- Maladie coronarienne : 34 (14 %).</li> <li>- Antécédent d'infarctus du myocarde : 18 (7,8 %).</li> <li>- Revascularisation de l'artère périphérique : 12 (5,2 %) carotide et 83 (37,5 %) artère du membre inférieur.</li> <li>- Traitement antiplaquettaire (à l'inclusion) : 211 (91,7 %), dont 21 (9,1 %) traitements antiplaquettaires doubles (DAPT).</li> <li>- Anticoagulant par voie orale : 40 patients (17,4 %).</li> <li>• <b>Caractéristiques d'intervention :</b> <ul style="list-style-type: none"> <li>- Contexte : hospitalisation 162 cas (70,4 %), clinique ambulatoire 68 cas (29,6 %).</li> <li>- Indication prédominante : claudication 147 cas (63,9 %).</li> <li>- Approche : 35 antégrades (15,3 %), 194 rétrogrades (84,7 %).</li> </ul> </li> <li>• <b>Principaux critères d'évaluation :</b> <ul style="list-style-type: none"> <li>- Critère d'évaluation combiné de l'innocuité (absence de complications majeures au niveau du membre du site d'accès dans les 6 heures suivant l'intervention) et de l'efficacité (hémostase réussie du site de ponction) atteint chez 215/226 (95,1 %) [IC à 95 % : 91,46 ; 97,55] patients dans l'ensemble d'analyse complet et chez 215/230 (93,5 %) [IC à 95 % : 89,47, 96,30] patients dans l'ensemble traité par FemoSeal™.</li> </ul> </li> </ul> |
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|  |  |  |  |  | <ul style="list-style-type: none"> <li>- Le critère d'évaluation de l'efficacité a été atteint chez 219/226 (96,9 %) [IC 93,7, 98,7] patients.</li> <li>- Critère d'évaluation de l'innocuité atteint chez 220/230 (95,2 %) [IC à 95 % : 92,15, 97,90] patients.</li> <li>• <b>Critères d'évaluation secondaires :</b> <ul style="list-style-type: none"> <li>- Absence de complications mineures au niveau du site d'accès pendant six heures après l'intervention atteinte chez 225/230 (97,8 %) [IC à 95 % : 95,00 ; 99,29] patients.</li> <li>- Absence de complications majeures et mineures au niveau du site d'accès de six heures à 30 jours après l'intervention atteinte chez 219/230 (95,2 %) [IC à 95 % : 91,60 ; 97,59] patients.</li> <li>- Temps moyen jusqu'à l'hémostase avec FemoSeal™ VCD : 0,42 (0,25 ; 0,50) minute.</li> <li>- Temps moyen avant la déambulation : 5,00 (4,54 ; 5,50) minutes.</li> <li>- Durée moyenne d'hospitalisation : 23,98 (22,72, 25,00) heures.</li> <li>- Utilisabilité du FemoSeal™ VCS : « facile » ou « très facile » à déployer dans 98,7 % des cas (« facile » à déployer dans 21 cas [9,2 %]), « très facile » à déployer dans 205 cas [89,5 %]) avec aucune résistance ou faible résistance lors du déploiement dans 226 cas (98,3 %).</li> </ul> </li> </ul> |
|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  |                                                                                                                                                                                                 |
|--|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | 152/230 (66,1 %) patients traités avec le fil-guide inclus dans le kit FemoSeal™ (0,038 po) et recommandé pour le FemoSeal™ sans déficiences de l'appareil ou événements indésirables signalés. |
|--|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

L'étude de 2006 a été menée pour confirmer la sécurité et l'efficacité du dispositif actuel avec un système d'administration amélioré et pour obtenir des commentaires sur le mode d'emploi et le programme de formation du FemoSeal™ VCS. L'étude incluait 100 patients et le critère d'évaluation principal était de savoir si l'hémostase était atteinte ou si des compressions manuelles ou mécaniques supplémentaires étaient nécessaires. Cette étude a conclu que l'application du FemoSeal™ VCS a réussi dans la majorité des cas (91 % ont obtenu une hémostase immédiate).

L'étude de 2008 a recruté 50 patients pour évaluer la sécurité et les performances du FemoSeal™ VCS lorsqu'il est utilisé pendant une routine clinique normale chez des patients subissant un cathétérisme cardiaque avec un introducteur 7 Fr. Le critère d'évaluation principal de l'étude était de recueillir des données sur le délai avant l'hémostase et le délai avant la déambulation sans compression supplémentaire (manuelle ou mécanique). Les résultats de l'étude ont conclu que le délai moyen avant l'hémostase était de 57,8 secondes et que tous les patients ont déambulé après 4 heures de repos au lit.

L'étude de 2009 visait à évaluer le nouvel emballage du FemoSeal™ VCS. Vingt-cinq patients ont été inclus dans l'étude. Le critère d'évaluation principal était de savoir si l'utilisateur rencontrait des problèmes avec l'emballage. Les utilisateurs n'ont noté aucun problème concernant le nouvel emballage du FemoSeal™ VCS. Cette étude a également recueilli des données sur le temps écoulé avant l'hémostase.

L'objectif de cette étude de 2022 était de démontrer de manière proactive l'innocuité et l'efficacité du FemoSeal VCS dans l'obtention de l'hémostase du site d'accès à l'artère fémorale commune (AFC) chez des sujets du monde réel subissant des procédures endovasculaires percutanées. 230 patients ont été inclus dans l'étude. Les principaux critères d'évaluation de l'étude sont la réussite de la procédure (c'est-à-dire l'hémostase réussie du site de ponction) et la diminution des complications majeures (par exemple, lésion vasculaire, saignement lié au site d'accès, infection du site d'accès, compression manuelle répétée et nouvelle ischémie ipsilatérale aiguë de la jambe liée au site d'accès). L'étude a conclu que le FemoSeal™ VCS fonctionne bien dans des environnements concrets, permet une hémostase efficace et de faibles taux de complications au niveau du site d'accès pour les patients subissant des interventions endovasculaires périphériques. Il se révèle performant, avec un délai pour atteindre l'hémostase



court et un bon retour d'information de l'opérateur, ce qui en fait un appareil précieux pour la fermeture de l'accès fémoral.

### 1.4.3 Résumé des données issues du suivi clinique post-commercialisation

#### 1.4.3.1 Suivi clinique post-commercialisation terminé

Un résumé des activités de suivi clinique post-commercialisation réalisées est décrit dans le **Tableau 1.7** ci-dessous.

**Tableau 1.7. Activités de suivi clinique post-commercialisation**

| Activités de suivi clinique post-commercialisation terminées              |             |                                                                    |                                                                                                                                                                                                           |                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|---------------------------------------------------------------------------|-------------|--------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Nom de l'activité                                                         | Année/CI    | Type d'étude                                                       | Objectifs                                                                                                                                                                                                 | Étapes clés                                                                                                                                                               | Critères d'acceptation potentielle                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021<br>TMC | Enquête clinique post-commercialisation – enquête de haute qualité | Enquête post-commercialisation visant à recueillir des commentaires prospectifs concernant l'utilisation du dispositif de fermeture vasculaire FemoSeal™ distribué sur les marchés de l'Union européenne. | <ul style="list-style-type: none"> <li>120 cas</li> <li>8 médecins uniques ayant &gt; 5 ans d'expérience</li> <li>Plusieurs pays en Europe</li> </ul>                     | <b>Évaluation du dispositif sur une échelle de 1 à 5 – Déclarations de l'étude</b> <ul style="list-style-type: none"> <li>Critères d'acceptation <ul style="list-style-type: none"> <li>Les notations de 3 - 5 sont jugées favorables</li> <li>Toutes les déclarations doivent avoir un retour positif <math>\geq 80\%</math></li> </ul> </li> <li>Résultats <ul style="list-style-type: none"> <li>Aucune déclaration de l'étude n'a reçu &gt; 20 % de réponses défavorables</li> <li>Aucune plainte concernant le produit n'a été introduite</li> </ul> </li> </ul> |
| 20210298 – 0.035" and 0038" Guidewire Clinical Survey Report (2021)       | 2021<br>TMC | Enquête clinique post-commercialisation – enquête de haute qualité | Enquête post-commercialisation visant à recueillir des commentaires prospectifs concernant                                                                                                                | <ul style="list-style-type: none"> <li>Enquêtes pour le câble de 0,035 po <ul style="list-style-type: none"> <li>106 enquêtes</li> <li>64 médecins</li> </ul> </li> </ul> | <b>Évaluation du dispositif sur une échelle de 1 à 5 – Déclarations de l'étude</b> <ul style="list-style-type: none"> <li>Critères d'acceptation <ul style="list-style-type: none"> <li>Les notations de 3 - 5 sont</li> </ul> </li> </ul>                                                                                                                                                                                                                                                                                                                            |

| Activités de suivi clinique post-commercialisation terminées                                                                    |                         |                                                                    |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|---------------------------------------------------------------------------------------------------------------------------------|-------------------------|--------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                 |                         |                                                                    | l'utilisation du guide de 0,035 po inclus avec le dispositif de fermeture vasculaire (VCD) Angio-Seal™ VIP 6Fr et du guide de 0,038 po inclus avec le VCD Angio-Seal™ VIP 8Fr et le système de fermeture vasculaire FemoSeal distribués sur les marchés de l'Union européenne. | <ul style="list-style-type: none"> <li>Enquêtes pour le câble de 0,038 po <ul style="list-style-type: none"> <li>109 enquêtes</li> <li>55 médecins</li> </ul> </li> <li>12 enquêtes rétrospectives</li> </ul>                                                                                                                                                 | <p>jugées favorables</p> <ul style="list-style-type: none"> <li>Toutes les déclarations doivent avoir un retour positif <math>\geq 80\%</math></li> <li>Résultats <ul style="list-style-type: none"> <li>Tous les fils-guides ont reçu des évaluations acceptables</li> <li>Aucune plainte concernant le produit n'a été introduite</li> </ul> </li> </ul>                                                                                                                                                                                                                                                              |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024<br><br>TMC/TE | Enquête clinique post-commercialisation – enquête de haute qualité | Recueillir de manière prospective les commentaires relatifs à l'utilisation du FemoSeal VCS avec des fils-guides distribués sur le marché européen.                                                                                                                            | <ul style="list-style-type: none"> <li>126 enquêtes <ul style="list-style-type: none"> <li>7 sites</li> <li>5 pays</li> </ul> </li> <li>14 novembre 2023 – 11 juin 2024</li> <li>Spécialité médicale du médecin : <ul style="list-style-type: none"> <li>Chirurgien vasculaire</li> <li>Radiologue interventionnel</li> <li>Angiologie</li> </ul> </li> </ul> | <p><b>Évaluation du dispositif sur une échelle de 1 à 5 – Déclarations de l'étude</b></p> <ul style="list-style-type: none"> <li>Critères d'acceptation <ul style="list-style-type: none"> <li>Les notations de 3 - 5 sont jugées favorables</li> <li>Toutes les déclarations doivent avoir un retour positif <math>\geq 80\%</math></li> <li>Si des événements indésirables se produisent dans le cadre de cette enquête, ils doivent être ceux anticipés par la gestion des risques.</li> </ul> </li> <li>Données des patients <ul style="list-style-type: none"> <li>Femmes : 29,4 % (37/126)</li> </ul> </li> </ul> |

| Activités de suivi clinique post-commercialisation terminées |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|--------------------------------------------------------------|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                              |  |  |  |  | <ul style="list-style-type: none"> <li>○ Hommes :<br/>69,8 %<br/>(88/126)</li> <li>○ Sexe non divulgué : 0,8<br/>(1/126)</li> <li>○ Âge<br/>&gt; 75 ans :<br/>31,7 %</li> <li>• Résultats <ul style="list-style-type: none"> <li>○ Fil-guide fourni avec le FemoSeal™ VCS :<br/>101/126<br/>(80,2 %).</li> <li>○ Durée de la procédure (minutes) :<br/>63,4 (36,6) (moyenne (SD)) ; 57,0 (36,0 - 81,0) (moyenne (IQR))</li> <li>○ Toutes les évaluations des performances du FemoSeal™ VCS étaient favorables.</li> <li>○ Toutes les évaluations du fil-guide fourni par le FemoSeal™ VCS étaient favorables.</li> <li>○ Un événement indésirable (0,8 %) : les disques FemoSeal™ VCS n'étaient pas bien</li> </ul> </li> </ul> |

| Activités de suivi clinique post-commercialisation terminées |  |  |  |  |                                                                                                                                                                                                   |
|--------------------------------------------------------------|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                              |  |  |  |  | alignés, probablement en raison de l'utilisation d'un fil-guide rigide (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 pouce) nécessitant une compression manuelle pour obtenir l'hémostase. |

Terumo Medical Corporation a réalisé trois enquêtes de haute qualité auprès des utilisateurs médicaux au cours de la période sous revue en cours (du 1<sup>er</sup> septembre 2019 au 31 août 2024).

Les enquêtes cliniques sur le FemoSeal™ ont recueilli des données cliniques proactives concernant la sécurité et les performances du FemoSeal™ VCS pendant l'utilisation clinique. L'enquête comprenait des questions portant sur le dispositif dans son ensemble et ses accessoires, notamment le fil-guide de 0,038" et ses interactions directes. Les études cliniques sur le fil-guide ont recueilli des données cliniques proactives relatives à la sécurité et aux performances pendant l'utilisation clinique du fil-guide de 0,038" fourni avec le FemoSeal™ VCS. Les questions de l'enquête portaient spécifiquement sur l'utilisation générale du fil-guide, allant de l'insertion dans le système vasculaire à l'insertion dans l'introducteur, en passant par le retrait du fil-guide.

Le FemoSeal™ VCS et le fil-guide de 0,038" inclus avec le dispositif ont reçu toutes les notes admissibles et six (6) plaintes ont été déposées pour le dispositif et neuf (9) non-plaintes pour le fil-guide sur la base de l'évaluation des observations reçues lors des études cliniques de haute qualité. Les plaintes ont été évaluées pour le dispositif FemoSeal et le fil-guide et ont été évaluées dans le cadre du processus de surveillance post-commercialisation de Terumo. Aucun nouveau risque ni niveau de risque n'a été identifié.

Une enquête auprès des utilisateurs de médecins a été réalisée en 2024 dans le cadre des activités de PMCF. Les résultats de l'enquête ont démontré que l'évaluation des performances et de la

sécurité du FemoSeal™ VCS étaient globalement très favorables. La compatibilité d'autres fils-guides que le guide standard fourni avec le FemoSeal™ VCS a également été démontrée.

#### **1.4.3.2 Suivi clinique post-commercialisation en cours/planifié**

TMC a deux activités de suivi clinique post-commercialisation en cours/planifiées. Une étude clinique sera réalisée pour recueillir de manière prospective des observations concernant l'utilisation du fil-guide avec le FemoSeal VCS distribué sur le marché de l'UE. L'enquête sera complétée par des médecins dans le but d'étudier les fils-guides qu'ils ont utilisés pendant la procédure. L'objectif de cette enquête est de combler une lacune identifiée comme étant le manque de documentation et de commentaires d'examineurs externes sur la compatibilité du FemoSeal™ VCS avec l'utilisation d'autres fils-guides de marques autres que Terumo. Le retour d'informations comprend les résultats techniques, les performances cliniques et la sécurité liés aux performances du dispositif avec différents fils-guides.

#### **1.4.4 Résumé des données issues de l'examen systématique de la littérature**

Terumo Medical Corporation procède à des revues systématiques de la littérature afin de recueillir et d'évaluer les données de sécurité et de performances cliniques issues des études publiées sur le FemoSeal™ VCS et/ou des dispositifs similaires. L'objectif de cette étude annuelle de la littérature est d'identifier les effets indésirables non connus, de surveiller les effets indésirables connus, de détecter les risques émergents et d'identifier une mauvaise utilisation systématique ou une utilisation non prévue du FemoSeal™ VCS.

La revue systématique de la littérature la plus récente, qui couvre la période allant du 1<sup>er</sup> septembre 2019 au 31 août 2024, a permis d'identifier 29 études publiées qui ont fourni des données de sécurité et de performances cliniques sur le FemoSeal™ VCS. Vingt-trois références ont signalé une utilisation prévue du FemoSeal™ VCS et une utilisation non prévue a été signalée dans neuf études. Dans l'ensemble, la revue dans la littérature d'études spécifiques à l'utilisation du FemoSeal™ VCS montre une population en cours d'étude représentative des patients de l'UE subissant des procédures de cathétérisme vasculaire percutané. Voir la **Section 3** pour voir une liste de ces 23 publications examinées par des pairs.

Les performances cliniques ont été évaluées par les mesures suivantes :

- Le délai avant l'hémostase est meilleur ou comparable à celui de la technique de pointe pour la fermeture percutanée de l'artère fémorale.
- Le délai avant la déambulation est meilleur ou comparable à celui de la technique de pointe pour la fermeture percutanée de l'artère fémorale.
- Le taux de complications postopératoires est comparable ou inférieur aux normes de soins actuelles.

Sur la base de ces indicateurs de performance clinique, les données de cette revue de la littérature ont démontré que le FemoSeal™ VCS peut être utilisé avec succès pour fermer la ponction dans l'artère fémorale (artériotomie) chez des patients qui ont subi un cathétérisme percutané à l'aide d'un introducteur 7 Fr ou de plus petite taille. Une hémostase complète a été obtenue chez la majorité des patients (79,65 - 100 %) des cas et a été associée à un délai médian jusqu'à l'hémostase de 0,5 min et un délai moyen jusqu'à la sortie de l'hôpital de 3 jours. Entre 69,2 et 86,7 % des patients ont pu déambuler 5 heures après la fermeture, avec un repos au lit postopératoire moyen de 349 min. Une défaillance du FemoSeal™ VCS a été observée dans 3,68 à 4 % des cas et une compression manuelle supplémentaire a été nécessaire dans 0,9 à 4,4 % des procédures.

La sécurité clinique a été évaluée par le biais des événements indésirables, y compris, mais sans s'y limiter :

- Saignement
- Hématome
- Pseudo-anévrisme
- Ecchymoses
- Fistule artérioveineuse
- Infection
- Décès

Pour chacun de ces événements indésirables, le taux d'occurrence rapporté pour le FemoSeal™ VCS dans les études incluses était inférieur ou comparable aux taux rapportés historiquement pour la compression manuelle et les autres appareils de fermeture vasculaire.

Aucun événement indésirable n'a été identifié lors de l'examen de 10 rapports d'intervention, car aucun risque nouveau, non anticipé, émergent ou inacceptable n'a été identifié.

L'efficacité globale de l'utilisation du FemoSeal™ VCS pendant l'angiographie diagnostique ou les interventions chirurgicales dépend de plusieurs facteurs tels que le sexe, l'âge, l'anatomie du patient, les comorbidités, le positionnement anatomique du site de ponction, l'expérience du chirurgien, la méthode de déploiement du VCD, les soins postopératoires, etc. Outre le succès technique, y compris l'obtention de l'hémostase, le FemoSeal™ VCS a offert des bénéfices cliniques par rapport à la fermeture vasculaire après ponction artérielle fémorale, tels que la réduction du délai jusqu'à l'hémostase et la réduction du délai avant la déambulation. Le score des performances du FemoSeal™ VCS sont cohérents avec ceux attendus pour ce type d'appareil lorsqu'il est utilisé comme prévu. Certaines des références récupérées au cours de la période de recherche actuelle ont montré l'utilisation de l'appareil du sujet dans un endroit anatomique autre que l'artère fémorale commune et pour la fermeture d'artériotomies > 7 Fr, ce qui est considéré comme une utilisation non prévue.

Lors de l'examen, aucun effet secondaire inconnu, aucun risque émergent ni aucune mauvaise utilisation systématique possible de l'appareil n'ont été identifiés. Cependant, si le FemoSeal™ VCS est utilisé avec précaution par des médecins formés, le dispositif médical fonctionne comme un appareil clinique utile et nécessaire. Globalement, le traitement cible et donc le FemoSeal™ VCS répondent au besoin clinique qui existe actuellement dans le traitement des complications liées à l'accès vasculaire.

Dans l'ensemble, les données de cette revue de la littérature n'ont pas mis en évidence de problèmes de performances ou de sécurité précédemment inconnus dans le contexte clinique, ni d'effets défavorables survenus à des taux plus élevés que celui prévu/acceptable. Par conséquent, il ressort de cette revue de la littérature que le FemoSeal™ VCS, lorsqu'il est utilisé pour fournir une compression pour atteindre l'hémostase au niveau de l'artériotomie après un cathétérisme percutané, continue à fonctionner comme prévu et n'est pas associé à des événements graves de sécurité.

#### **1.4.5 Résumé des données issues de la surveillance post-commercialisation**

Un système PMS proactif est en place et un examen de toutes les réclamations est effectué tous les mois et conformément aux procédures de fabrication internes. Les données relatives aux réclamations ont été analysées entre le 1<sup>er</sup> septembre 2019 et le 31 août 2024. Dans l'ensemble, 28 rapports de matériovigilance (MDV) et 476 plaintes de clients ont été soumis au fabricant. Sur les 28 rapports MDV, 27 étaient liés à des événements indésirables et un à un dysfonctionnement de l'appareil. Il y a eu deux décès au cours de la période considérée, mais aucun des décès signalés n'a été jugé lié à l'appareil concerné. Parmi les 476 plaintes adressées au fabricant, les raisons les plus fréquentes des plaintes étaient des difficultés de déploiement (146 occurrences, taux d'occurrence de 0,0142 %). Le mode de défaillance des événements de retrait est le deuxième le plus fréquent avec un taux de 0,0126 % (130 événements).

Le système de fermeture vasculaire FemoSeal™ a été vendu à plus de 1 030 136 exemplaires dont 827 843 dans l'Espace économique européen. La fréquence des plaintes sur la base des ventes dans le monde est de 0,046 %. Le taux global de plaintes de clients est très faible. Aucun nouveau risque non inclus dans le mode d'emploi et la documentation sur les risques n'a été identifié.

Les taux d'occurrence des effets secondaires indésirables sont présentés dans le **Tableau 1.2**. Aucun nouveau risque inattendu, émergent ou inacceptable n'a été identifié. Il n'y a pas eu d'augmentation significative de la fréquence ou de la gravité des effets secondaires indésirables connus.

#### **1.4.6 Résumé global des performances cliniques et de sécurité**

Le FemoSeal™ VCS est indiqué pour la fermeture de la ponction artérielle dans l'artère fémorale commune (artériotomie) chez les patients ayant subi un cathétérisme percutané à l'aide

d'un introducteur de 7,33 mm (7F) ou moins. Cette évaluation clinique se base sur une analyse complète des données cliniques et de la littérature disponibles avant et après commercialisation, pertinentes pour l'utilisation prévue du FemoSeal™ VCS.

Une revue complète de la littérature publiée a été menée entre le 1<sup>er</sup> septembre 2019 et le 31 août 2024. Le faisceau des preuves comprenait 29 études pour le FemoSeal™ VCS. Les preuves fournies dans l'évaluation clinique concluent que, lorsqu'il est utilisé comme indiqué, le dispositif du sujet est sûr et efficace et que tous les risques ou effets secondaires indésirables, qui peuvent être associés à l'appareil dans des conditions normales d'utilisation, constituent des risques acceptables lorsqu'ils sont comparés aux avantages pour le patient. Le score des performances des appareils sujets sont cohérents avec ceux attendus pour ce type d'appareil lorsqu'il est utilisé comme prévu.

Les effets secondaires indésirables potentiels associés à l'utilisation du FemoSeal™ VCS incluent les événements indésirables fréquemment signalés avec d'autres moyens de fermeture d'artériotomie, par exemple, saignement et hématome. Dans l'ensemble, les taux d'occurrence des événements indésirables rapportés avec l'utilisation du FemoSeal™ VCS sont similaires aux taux rapportés avec la compression manuelle et les dispositifs de fermeture vasculaire similaires. Plus précisément, pour les saignements et les hématomes, les taux rapportés pour le FemoSeal™ VCS sont inférieurs aux taux rapportés pour les dispositifs de fermeture vasculaire similaires. Chacun des événements indésirables signalés, issus à la fois de la littérature publiée et de la surveillance post-commercialisation, avait été précédemment identifié (voir **Section 1.3**).

Les données existantes concernant la sécurité et les performances cliniques du FemoSeal VCS suggèrent que les bénéfices pour le patient de l'utilisation de ce dispositif de fermeture vasculaire l'emportent sur les risques potentiels lorsqu'il est utilisé conformément au mode d'emploi.

Comme indiqué dans les paragraphes précédents, les données fournies pour le FemoSeal™ VCS démontrent la concordance entre les données relatives au dispositif évalué (par exemple, l'utilisation du dispositif, les résultats en matière de sécurité, les performances et les bénéfices cliniques), les dispositifs équivalents identifiés et les données liées à des dispositifs similaires répertoriés dans les données les plus récentes.

L'analyse croisée des données de sécurité n'a pas permis d'identifier de différences entre :

- Les données mentionnées dans les informations les plus récentes
- Les données spécifiques au dispositif analysé
- Les données mentionnées dans le(s) dossier(s) de gestion des risques
- Les données mentionnées sur l'étiquetage et/ou le mode d'emploi (les risques résiduels à transmettre à l'utilisateur sont traités)



La sécurité clinique a été démontrée par de faibles taux de complications identifiées dans la littérature clinique examinée par des pairs, des études cliniques parrainées par des sociétés, l'examen des données post-commercialisation associées à l'absence de retrait du marché. Aucun problème de performances n'a été relevé. La littérature examinée indiquait une utilisation du dispositif FemoSeal™ VCS conforme à l'utilisation prévue par le fabricant.

### **1.5 Autres diagnostics ou traitements possibles**

La compression manuelle est traditionnellement utilisée pour obtenir une hémostase au niveau du site d'artériotomie après un cathétérisme vasculaire. La compression manuelle a été associée à l'immobilisation du patient pendant de longues périodes (jusqu'à 8 heures après une procédure), à une gêne importante et à des séjours prolongés à l'hôpital. Une étude systématique récente a révélé que le délai moyen pour atteindre l'hémostase avec compression manuelle était de 20,8 minutes. <sup>1</sup>

Les dispositifs hémostatiques externes qui appliquent une compression mécanique au niveau du site d'artériotomie sont des solutions de remplacement à la compression manuelle. Ces dispositifs ne raccourcissent pas le délai avant l'hémostase ou la déambulation, mais réduisent les besoins en personnel en remplaçant la compression manuelle par la compression mécanique. Les taux d'événements indésirables associés à l'utilisation de la compression mécanique sont similaires à ceux de la compression manuelle.

Les appareils de fermeture vasculaire, comme le FemoSeal™ VCS, sont conçus pour fermer l'artériotomie. Ils visent à réduire le temps d'hémostase et à permettre une déambulation plus précoce. Une étude systématique récente incluant 13 dispositifs disponibles sur le marché a révélé que le délai moyen pour atteindre l'hémostase avec un dispositif de fermeture vasculaire était de 5,4 minutes. Le délai moyen pour atteindre l'hémostase pour les différents dispositifs de fermeture vasculaire allait de 1 minute (FemoSeal™ VCS) à 14 minutes ; le délai pour la majorité des appareils étant compris entre 4 et 10 minutes. <sup>1</sup>

Les événements indésirables fréquemment rapportés liés à la fermeture du site d'artériotomie, avec des compressions manuelles, des appareils hémostatiques externes ou des dispositifs de fermeture vasculaire, comprennent un hématome, un saignement au niveau du site d'accès, un pseudo-anévrisme, une fistule artérioveineuse et une infection. La même étude systématique (34 études contrôlées randomisées, 14 401 patients) a révélé que les taux d'événements indésirables étaient similaires entre la compression manuelle et l'utilisation de dispositifs de fermeture vasculaire. Toutefois, l'étude a révélé que les saignements avaient tendance à être un peu plus élevés avec les dispositifs de fermeture vasculaire. <sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Suggestions de profils d'utilisateurs et de formations

Les utilisateurs auxquels le FemoSeal™ Vascular Closure System est destiné sont des médecins qui ont suivi une formation leur permettant d'effectuer un accès et une fermeture artériels pour des procédures endovasculaires par le biais de l'artère fémorale commune et qui ont participé à un programme de formation pour médecins FemoSeal™ de Terumo Medical Corporation.

## 1.7 Normes communes et harmonisées pertinentes

| Référence standard | Année actuelle de conformité/rév. | Description                                                                                                                              |
|--------------------|-----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070          | 2014/AMD1:2018                    | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070       | 2014/A1:2018                      | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance       | 20 mai 2021                       | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052         | 2015                              | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213         | 2017                              | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503         | 2020                              | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182         | 2019                              | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |
| EN ISO 13485       | 2016/A11:2021                     | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 13485          | 2016                              | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |

| Référence standard | Année actuelle de conformité/rév. | Description                                                                                                                                                              |
|--------------------|-----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14644-1        | 2015                              | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1     | 2015                              | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2        | 2015                              | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2     | 2015                              | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3        | 2019                              | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3     | 2019                              | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1        | 2003                              | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1     | 2003                              | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2        | 2003/TC1:2004                     | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| EN ISO 14698-2     | 2003/TC 1/2004                    | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| USP <788>          | S.O                               | PARTICULATE MATTER IN INJECTIONS                                                                                                                                         |

| Référence standard               | Année actuelle de conformité/rév. | Description                                                                                                          |
|----------------------------------|-----------------------------------|----------------------------------------------------------------------------------------------------------------------|
| Pharmacopée européenne<br>2/9/19 | S/O                               | Particulate Contamination: Sub-Visible Particles                                                                     |
| IEC 62366-1                      | 2015                              | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN 62366-1                       | 2015                              | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN ISO 14971                     | 2019/A11:2021                     | Medical devices — Application of risk management to Medical devices                                                  |
| ISO 14971                        | 2019                              | Medical devices — Application of risk management to Medical devices                                                  |
| ASTM F1980                       | 2016                              | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1                   | 2020                              | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1                      | 2018                              | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2                   | 2006                              | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2                      | 2006                              | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3                   | 2014                              | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3                      | 2014                              | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4                   | 2017                              | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4                      | 2017                              | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |

| Référence standard | Année actuelle de conformité/rév. | Description                                                                                                                                |
|--------------------|-----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-5     | 2009                              | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                                         |
| ISO 10993-5        | 2009                              | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                                         |
| EN ISO 10993-6     | 2016                              | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| ISO 10993-6        | 2016                              | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| EN ISO 10993-10    | 2023                              | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| ISO 10993-10       | 2021                              | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| EN ISO 10993-11    | 2018                              | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| ISO 10993-11       | 2017                              | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| EN ISO 10993-12    | 2021                              | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| ISO 10993-12       | 2021                              | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| EN ISO 10993-17    | 2009                              | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17       | 2002                              | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18       | 2020/A1:2022                      | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |

| Référence standard | Année actuelle de conformité/rév. | Description                                                                                                                                                                  |
|--------------------|-----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-18    | 2020/A1:2022                      | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| ISO 10993-23       | 2021                              | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23       | 2021                              | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382         | 2018                              | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756          | 2017                              | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>           | S/O                               | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>          | S/O                               | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72     | 2019                              | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| ISO 11135          | 2014/A1:2019                      | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135          | 2014/A1:2018                      | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7     | 2008/A1:2022                      | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |

| Référence standard | Année actuelle de conformité/rév. | Description                                                                                                                                                     |
|--------------------|-----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-7        | 2008/A1:2019                      | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                               |
| EN 556-1           | 2024                              | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices |
| ISO 11737-1        | 2018/A1:2021                      | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11737-1        | 2018/A1:2021                      | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11138-1        | 2017                              | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-1        | 2017                              | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-2        | 2017                              | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 11138-2        | 2017                              | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 15223-1        | 2016                              | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| ISO 15223-1        | 2016                              | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| EN 1041            | 2008/A1:2013                      | Information supplied by the manufacturer of medical devices                                                                                                     |
| ISO 11607-1        | 2020/A1:2023                      | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                         |

| Référence standard   | Année actuelle de conformité/rév. | Description                                                                                                                                                                |
|----------------------|-----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11607-1          | 2019/A1:2023                      | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| EN ISO 11607-2       | 2020/A1:2023                      | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ISO 11607-2          | 2019/A1:2023                      | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169           | 2016                              | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M-16 | 2016                              | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825           | 2018                              | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096           | 2011 (R 2019)                     | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M-15     | 2015                              | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24         | 2021                              | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3          | 2020                              | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |
| MDCG 2020-8          | 2020                              | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                             |
| MDCG 2020-7          | 2020                              | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                          |



| Référence standard | Année actuelle de conformité/rév. | Description                                                                                                                                                                                                                                                   |
|--------------------|-----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-6        | 2020                              | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                                                                                                          |
| MDCG 2019-9 v1     | 2022                              | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                                                                                      |
| MDCG 2019-8 v2     | 2020                              | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15       | 2020                              | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11       | 2021                              | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19       | 2021                              | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4     | 2021                              | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2        | 2019                              | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1        | 2019                              | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7        | 2018                              | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6        | 2018                              | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |

| Référence standard      | Année actuelle de conformité/rév. | Description                                                                                                                                                                                   |
|-------------------------|-----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2018-4             | 2018                              | MDCG 2018-4 Annex: UDI database<br>Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                               |
| MDCG 2018-3<br>v1       | 2020                              | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25            | 2021                              | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2,12-2<br>Rév. 2 | 2012                              | Guidance document medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                        |

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### 3.0 HISTORIQUE DES REVISIONS

| Numéro de révision<br>SSCP   | Date de<br>publication | Description de la<br>modification                                                                            | Révision validée par<br>l'organisme notifié                                                                                                                                                                                                                                                                                                                                                                                                            |
|------------------------------|------------------------|--------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022                 | 20 janvier 2023        | Publication initiale, lors de la certification CE conformément au règlement relatif aux dispositifs médicaux | <p><input checked="" type="checkbox"/> Oui</p> <p>Langue de validation : English</p> <p><input checked="" type="checkbox"/> Non (applicable uniquement pour les dispositifs implantables de classe IIa ou certains dispositifs de classe IIb (MDR, article 52(4) 2e paragraphe) pour lesquels le SSCP n'a pas encore été validé par la NB)</p> <p><input type="checkbox"/> Autre (précisez) :</p>                                                      |
| SSCP-FS-2023 –<br>Révision 1 | 15 mars 2024           | Mise à jour pour la période du 1 <sup>er</sup> janvier 2019 au 31 décembre 2023.                             | <p><input checked="" type="checkbox"/> Oui</p> <p>Langue de validation : English</p> <p><input type="checkbox"/> Non (applicable uniquement pour les dispositifs implantables de classe IIa ou certains dispositifs de classe IIb [règlement relatif aux dispositifs médicaux, article 52(4) 2<sup>e</sup> paragraphe] pour lesquels le SSCP n'a pas encore été validé par l'organisme notifié)</p> <p><input type="checkbox"/> Autre (précisez) :</p> |
| SSCP-FS-2024<br>Révision 1   |                        | Mise à jour pour la période du 1 <sup>er</sup> septembre 2019 au 31 août 2024.                               | <p><input type="checkbox"/> Oui</p> <p>Langue de validation : English</p> <p><input type="checkbox"/> Non (applicable uniquement pour les dispositifs implantables de classe IIa ou certains dispositifs de classe IIb [règlement relatif aux dispositifs médicaux,</p>                                                                                                                                                                                |

|                                    |                      |                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|------------------------------------|----------------------|-----------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                    |                      |                                                                             | <p>article 52(4) 2<sup>e</sup> paragraphe]<br/>pour lesquels le SSCP n'a pas<br/>encore été validé par<br/>l'organisme notifié)</p> <p><input type="checkbox"/> Autre (précisez) :</p>                                                                                                                                                                                                                                                                                                         |
| <p>SSCP-FS-2024<br/>Révision 2</p> | <p>June 20, 2025</p> | <p>Révisé sur la base des<br/>requêtes de l'ANSI pour<br/>la validation</p> | <p><input checked="" type="checkbox"/> Oui</p> <p>Langue de validation :<br/>English</p> <p><input type="checkbox"/> Non (applicable uniquement<br/>pour les dispositifs implantables<br/>de classe IIa ou certains<br/>dispositifs de classe IIb<br/>[règlement relatif aux<br/>dispositifs médicaux,<br/>article 52(4) 2<sup>e</sup> paragraphe]<br/>pour lesquels le SSCP n'a pas<br/>encore été validé par<br/>l'organisme notifié)</p> <p><input type="checkbox"/> Autre (précisez) :</p> |

**Περίληψη των χαρακτηριστικών ασφάλειας και  
των κλινικών επιδόσεων**

**FemoSeal™ Vascular Closure System**

|                                                                                                 |                                                                                             |
|-------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|
| <b>Κατασκευαστής</b>                                                                            | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 USA         |
| <b>Ενιαίος αριθμός καταχώρισης<br/>(SRN) κατασκευαστή</b>                                       | US-MF-000019594                                                                             |
| <b>Management Representative/PRRC</b>                                                           | Kimberly Feitl<br>Vice President, Quality                                                   |
| <b>Βασικό UDI-DI</b>                                                                            | 38970FS79                                                                                   |
| <b>Αριθμός EMDN</b>                                                                             | C900199 – Συστήματα αιμόστασης-Άλλο                                                         |
| <b>Κατηγορία ιατροτεχνολογικού<br/>προϊόντος</b>                                                | Κατηγορία III                                                                               |
| <b>Έτος κατά το οποίο το<br/>ιατροτεχνολογικό προϊόν έλαβε για<br/>πρώτη φορά τη σήμανση CE</b> | 2005                                                                                        |
| <b>Αντιπρόσωπος στην ΕΕ</b>                                                                     | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Βέλγιο<br>SRN: BE-AR-000001433 |
| <b>Κοινοποιημένος Οργανισμός</b>                                                                | NSAI<br>CE 0050                                                                             |



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Αυτή η περίληψη των χαρακτηριστικών ασφάλειας και των κλινικών επιδόσεων (SSCP) προορίζεται για την παροχή πρόσβασης στο κοινό σε μια επικαιροποιημένη περίληψη των κύριων πτυχών της ασφάλειας και των κλινικών επιδόσεων του FemoSeal™ Vascular Closure System (VCS).

Μια περίληψη των χαρακτηριστικών ασφάλειας και κλινικών επιδόσεων του ιατροτεχνολογικού προϊόντος για χρήστες/επαγγελματίες υγειονομικής περίθαλψης παρέχεται παρακάτω στην **Ενότητα 1.0**.

## **1.0 ΣΥΝΟΨΗ ΓΙΑ ΧΡΗΣΤΕΣ / ΕΠΑΓΓΕΛΜΑΤΙΕΣ ΥΓΕΙΟΝΟΜΙΚΗΣ ΠΕΡΙΘΑΛΨΗΣ**

Η SSCP δεν προορίζεται να αντικαταστήσει τις Οδηγίες χρήσης ως κύριο έγγραφο για τη διασφάλιση της ασφαλούς χρήσης του ιατροτεχνολογικού προϊόντος ούτε προορίζεται να παρέχει διαγνωστικές ή θεραπευτικές προτάσεις στους προβλεπόμενους χρήστες ή ασθενείς. Η SSCP δεν προορίζεται για την αντικατάσταση των υποχρεωτικών πληροφοριών στις κάρτες εμφυτεύματος ή σε άλλα υποχρεωτικά έγγραφα.

### **1.1 Προβλεπόμενη χρήση του ιατροτεχνολογικού προϊόντος**

#### **1.1.1 Προβλεπόμενη χρήση**

Το FemoSeal™ Vascular Closure System είναι ένα ιατροτεχνολογικό προϊόν που προορίζεται για τη σύγκλειση αρτηριακής διάτρησης μετά από διαδερμικό καθετηριασμό μέσω της κοινής μηριαίας αρτηρίας.

#### **1.1.2 Ενδείξεις χρήσης**

Το FemoSeal™ Vascular Closure System ενδείκνυται για χρήση στη σύγκλειση της διάτρησης της κοινής μηριαίας αρτηρίας (αρτηριοτομή) σε ασθενείς που έχουν υποβληθεί σε διαδερμικό καθετηριασμό με χρήση επεμβατικού θηκαριού 7F (2,33 mm) ή μικρότερου.

#### **1.1.3 Αντενδείξεις ή/και περιορισμοί**

Το FemoSeal™ Vascular Closure System αντενδείκνυται σε ασθενείς με αρτηριοτομές στις οποίες έχουν χρησιμοποιηθεί θηκάρια ή προϊόντα μεγαλύτερα από 7 F (2,33 mm).

#### **1.1.4 Στοχευόμενοι πληθυσμοί ασθενών**

Η ασφάλεια και η αποτελεσματικότητα του FemoSeal™ Vascular Closure System έχουν τεκμηριωθεί σε ασθενείς ηλικίας 18 ετών και άνω, οι οποίοι έχουν υποβληθεί σε διαδερμικό καθετηριασμό με χρήση επεμβατικού θηκαριού 7F (2,33 mm) ή μικρότερου.

#### **1.1.5 Ειδικοί πληθυσμοί ασθενών**

Η ασφάλεια και η αποτελεσματικότητα του FemoSeal™ Vascular Closure System δεν έχουν τεκμηριωθεί στους ακόλουθους πληθυσμούς ασθενών:

- Ασθενείς με προϋπάρχον αυτοάνοσο νόσημα.
- Ασθενείς που υποβάλλονται σε θεραπευτική θρομβόλυση.
- Ασθενείς με κλινικά σημαντική περιφερική αγγειακή νόσο.
- Ασθενείς με μη ελεγχόμενη υπέρταση (> 220 mmHg συστολική ή > 110 mmHg διαστολική).

- Ασθενείς με αιμορραγική διαταραχή, συμπεριλαμβανομένης της θρομβοπενίας (αριθμός αιμοπεταλίων < 100.000), ή αναιμία (Hgb < 10 mg/dl).
- Ασθενείς με εσωτερικό αυλό της κοινής μηριαίας αρτηρίας μικρότερο από 5 mm.
- Ασθενείς με νεφρική ή/και ηπατική δυσλειτουργία.
- Ασθενείς με άλλη σχετική συννοσηρότητα.
- Πληθυσμός με ειδική φυλετική ή/και εθνοτική καταγωγή.
- Ασθενείς που έχουν υποστεί έμφραγμα του μυοκαρδίου εντός 72 ωρών.
- Ασθενείς με αγγειακό μόσχευμα ή ενδοπρόθεση στο σημείο διάτρησης.
- Έγκυες ασθενείς ή ασθενείς που θηλάζουν.
- Ασθενείς κάτω των 18 ετών.

#### 1.1.6 Προβλεπόμενοι χρήστες

Οι προβλεπόμενοι χρήστες του FemoSeal™ Vascular Closure System είναι ιατροί με εκπαίδευση που τους επιτρέπει τη διεξαγωγή αρτηριακής πρόσβασης και σύγκλεισης για ενδοαγγειακές επεμβάσεις μέσω της κοινής μηριαίας αρτηρίας και έχουν συμμετάσχει σε ένα πρόγραμμα εκπαίδευσης ιατρών της Terumo Medical Corporation FemoSeal™.

## 1.2 Περιγραφή τεχνολογικού προϊόντος

### 1.2.1 Περιγραφή του ιατροτεχνολογικού προϊόντος

Το FemoSeal™ Vascular Closure System, το οποίο κατασκευάζεται από την Terumo Medical Corporation (TMC), είναι ένα απορροφήσιμο ιατροτεχνολογικό προϊόν σύγκλεισης αγγείων που έχει σχεδιαστεί για να επιτύχει την αιμόσταση της μηριαίας αρτηρίας μετά από διαδερμικό καθετηριασμό μέσω της κοινής μηριαίας αρτηρίας.

Τα στοιχεία σύγκλεισης του FemoSeal™ αποτελούνται από δύο απορροφήσιμους πολυμερείς δίσκους, την εσωτερική στεγανοποίηση και τον εξωτερικό δίσκο ασφάλισης, οι οποίοι συγκρατούνται μεταξύ τους από ένα απορροφήσιμο πολύκλωνο υλικό, στεγανοποιώντας έτσι μηχανικά την αρτηριοτομή (βλ. **Εικόνα 1.1** και **Εικόνα 1.2**). Μετά την έκπτυξη μέσω του θηκαριού περιβλήματος κώνου, ο εξωτερικός δίσκος ασφάλισης επικαλύπτεται επάνω στον πολύκλωνο άξονα, με αποτέλεσμα τη μηχανική σύγκλειση του σημείου διάτρησης μεταξύ του εσωτερικού και του εξωτερικού δίσκου ασφάλισης. Η εσωτερική στεγανοποίηση και ο εξωτερικός δίσκος ασφάλισης συγκρατούνται στη θέση τους μέσω τριβής στον πολύκλωνο

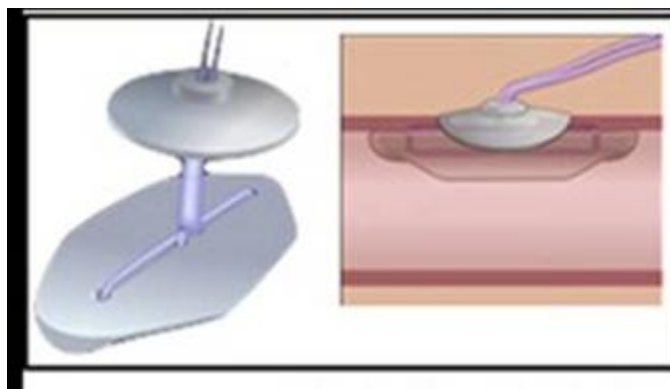
άξονα. Η αιμόσταση επιτυγχάνεται με μηχανικά μέσα. Τα στοιχεία σύγκλεισης αποδομούνται μέσω υδρόλυσης.

Τα εμφυτεύσιμα συστατικά σύγκλεισης, η εσωτερική στεγανοποίηση και ο εξωτερικός δίσκος ασφάλισης αποδομούνται εντός δεκαοκτώ (18) μηνών, ενώ το πολύκλωνο υλικό εκτιμάται ότι αποδομείται και απορροφάται μέσω υδρόλυσης από τον περιβάλλοντα ιστό μετά από δύο (2) έως τρία (3) έτη. Η ικανότητα των εμφυτεύσιμων στοιχείων σύγκλεισης να διατηρούν τη συμπίεση στην αρτηριοτομή έχει δοκιμαστεί για έως και οκτώ (8) ώρες. Τα προϊόντα αποδόμησης μεταβολίζονται και απεκκρίνονται στα ούρα ή εκλύονται ως διοξείδιο του άνθρακα μέσω των πνευμόνων. Δεν παρατηρήθηκαν επιπτώσεις συσσώρευσης σε μελέτες σε πειραματόζωα. Τα πρόσθετα στοιχεία του FemoSeal™ που θα έρθουν σε επαφή με ζωντανό ιστό ή αίμα στη διάρκεια της επέμβασης είναι το θηκάρι περιβλήματος κώνου, ο διαστολέας, ο σωλήνας επικάλυψης, ο προωθητήρας και το οδηγό σύρμα.

**Εικόνα 1.1 Εσωτερική στεγανοποίηση και εξωτερικός δίσκος ασφάλισης, αντίστοιχα**



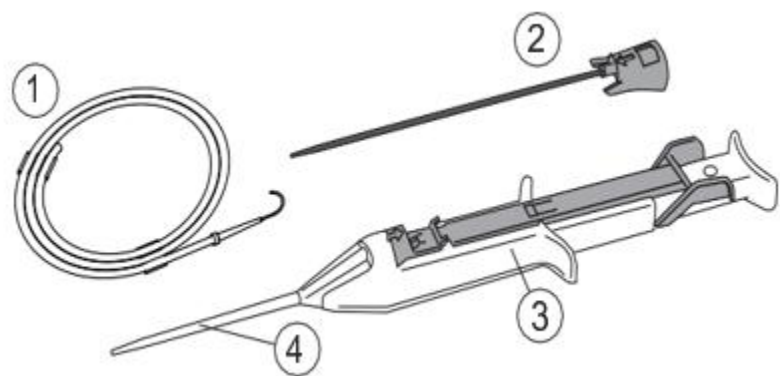
**Εικόνα 1.2 Εσωτερική στεγανοποίηση και εξωτερικός δίσκος ασφάλισης εκπτυγμένος**



Η μονάδα FemoSeal™ διατίθεται σε συσκευασία μαζί με έναν διαστολέα και ένα οδηγό σύρμα εξωτερικής διαμέτρου 0,038” (0,97 mm), μήκους 27,5” (70 cm) και ένα εργαλείο ευθυγράμμισης σχήματος J. Βλ. **Εικόνα 1.3** παρακάτω. Το οδηγό σύρμα βρίσκεται μέσα σε έναν σωλήνα πολυαιθυλενίου. Όλα τα εξαρτήματα είναι συσκευασμένα σε έναν σταθερό χάρτινο δίσκο. Η συσκευασία περιλαμβάνει επίσης την κάρτα εμφυτεύματος ασθενούς. Το FemoSeal™ Vascular Closure System δεν απαιτεί τη χρήση πρόσθετων παρελκομένων προκειμένου το

ιατροτεχνολογικό προϊόν να λειτουργεί όπως προορίζεται και το προϊόν προορίζεται για χρήση μόνο με τον διαστολέα και το οδηγό σύρμα που περιλαμβάνονται στη συσκευασία του προϊόντος.

**Εικόνα 1.3 Μονάδα FemoSeal™ VCS με οδηγό σύρμα και διαστολέα**



### 1.2.2 Πρώτες ύλες και συστατικά

Στον Πίνακα 1.1 παρακάτω παρατίθενται τα εξαρτήματα του FemoSeal™ VCS.

**Πίνακας 1.1 Πρώτες ύλες και εξαρτήματα του FemoSeal™ VCS**

| Αριθμός εξαρτήματος | Περιγραφή                                                                                    | Υλικά                                                                                                                                                                                         |
|---------------------|----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1                   | Οδηγό σύρμα 0,038" (0,97 mm) με εργαλείο σχήματος J για την ευθυγράμμιση του οδηγού σύρματος | Οδηγό σύρμα: Ανοξείδωτος χάλυβας 304<br><br>Εργαλείο ευθυγράμμισης σχήματος J: Πολυπροπυλένιο, μοβ χρωστική<br><br>Κλιπ: Πολυαιθυλένιο<br><br>Σωλήνωση: Πολυαιθυλένιο                         |
| 2                   | Διαστολέας FemoSeal                                                                          | Ομφαλός: Τετραϋδροφουράνιο, μπλε χρωστική, τερεφθαλικό πολυβουτυλένιο (PBT)<br><br>Σωλήνας: Πολυαιθυλένιο υψηλής πυκνότητας (HDPE), μαύρη χρωστική<br><br>Λιπαντικό: Σιλικόνη Dow Corning 360 |

|     |                 |                                                                             |                                                                                                                                                                                                                         |
|-----|-----------------|-----------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 3/4 | Μονάδα FemoSeal | Διαμορφωμένο RD7 – Εσωτερική στεγανοποίηση και εξωτερικός δίσκος ασφάλισης* | Συμπολυμερές μεταξύ γλυκολιδίου, ανθρακικού τριμεθυλενίου, ε-καπρολακτόνης και TMP: τριμεθυλολοπροπανίου (εκκινητής)                                                                                                    |
|     |                 | Πολύκλωνο *                                                                 | Τμηματοποιημένο συμπολυμερές μεταξύ L, L-λακτιδίου, ανθρακικού τριμεθυλενίου, ε-καπρολακτόνης και 1,3 προπανοδιόλης (εκκινητής)<br><br>Η επικάλυψη είναι συμπολυμερές μεταξύ γλυκολιδίου, ε-καπρολακτόνης και L-λυσίνης |
|     |                 | Σωλήνας επικάλυψης                                                          | Πολυπροπυλένιο                                                                                                                                                                                                          |
|     |                 | Προωθητήρας                                                                 | Ανοξείδωτος χάλυβας 304V                                                                                                                                                                                                |
|     |                 | Ολισθητήρας                                                                 | Τερεφθαλικό πολυβουτυλένιο (PBT)                                                                                                                                                                                        |
|     |                 | Περιβλήμα                                                                   | Τερεφθαλικό πολυβουτυλένιο (PBT)                                                                                                                                                                                        |
|     |                 | Κουμπί                                                                      | Τερεφθαλικό πολυβουτυλένιο (PBT)                                                                                                                                                                                        |
|     |                 | Καπάκι κουμπιού                                                             | Συμπολυμερές πολυοξυμεθυλενίου (POM)/πολυακετάλης                                                                                                                                                                       |
|     |                 | Χιτώνιο                                                                     | Τερεφθαλικό πολυβουτυλένιο (PBT)                                                                                                                                                                                        |
|     |                 | Αποστάτης                                                                   | Τερεφθαλικό πολυβουτυλένιο (PBT)                                                                                                                                                                                        |
|     |                 | Κόνος                                                                       | Πολυπροπυλένιο                                                                                                                                                                                                          |
|     |                 | Καπάκι περιβλήματος                                                         | Τερεφθαλικό πολυβουτυλένιο (PBT)                                                                                                                                                                                        |
|     |                 | Μηχανισμός συγκράτησης ασφάλειας                                            | Τερεφθαλικό πολυβουτυλένιο (PBT), μπλε χρωστική                                                                                                                                                                         |
|     |                 | Καπάκι χιτωνίου                                                             | Τερεφθαλικό πολυβουτυλένιο (PBT)                                                                                                                                                                                        |
|     |                 | Φλάντζα σωλήνα                                                              | Σιλικόνη Shore A 70                                                                                                                                                                                                     |
|     |                 | Φλάντζα περιβλήματος                                                        | Σιλικόνη shore A 50                                                                                                                                                                                                     |
|     |                 | Ελατήριο                                                                    | Ανοξείδωτος χάλυβας 302                                                                                                                                                                                                 |
|     |                 | Θηκάρι περιβλήματος κώνου                                                   | Πολυπροπυλένιο<br>Σιλικόνη Dow Corning 360, Εξάνιο                                                                                                                                                                      |

\* Εμφυτεύσιμο τμήμα του προϊόντος, τα εμφυτεύσιμα εξαρτήματα είναι ασφαλή για μαγνητική τομογραφία



Το FemoSeal™ VCS αποστειρώνεται με οξείδιο του αιθυλενίου (EO) και αποτελεί ιατροτεχνολογικό προϊόν μίας χρήσης. Το FemoSeal™ VCS είναι σχεδιασμένο με τέτοιο τρόπο ώστε να μην μπορεί να επαναχρησιμοποιηθεί.

### **Τρόπος λειτουργίας**

Το FemoSeal™ VCS προάγει τη μηχανική αιμόσταση εκπύσσοντας εμφυτεύσιμα στοιχεία σύγκλεισης εντός και εκτός της κοινής μηριαίας αρτηρίας. Ο μηχανισμός που αποτρέπει την αιμορραγία παρέχεται από την εσωτερική στεγανοποίηση, η οποία στεγανοποιεί το σημείο διάτρησης, και τον εξωτερικό δίσκο ασφάλισης που συγκρατεί την εσωτερική στεγανοποίηση στη θέση της.

#### **1.2.3 Κλινικό όφελος**

Το FemoSeal™ VCS παρέχει τα ακόλουθα κλινικά οφέλη σχετικά με τη σύγκλειση αγγείων μετά από διάτρηση της κοινής μηριαίας αρτηρίας:

- Μείωση χρόνου έως την αιμόσταση<sup>1</sup>
- Μείωση χρόνου έως το περιπατητικό στάδιο<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

#### **1.2.4 Προηγούμενη γενιά/ γενιές ή παραλλαγές**

- Η πρώτη έκδοση του FemoSeal™ VCS (αριθ. 11200) πωλήθηκε στην ευρωπαϊκή αγορά κατά τη διάρκεια του έτους 2005 και μέρους του 2006.
- Το τρέχον FemoSeal™ VCS (αριθ. 11202), με βελτιωμένο σύστημα χορήγησης, είναι διαθέσιμο στην αγορά από τις 28 Μαρτίου 2006.

#### **1.2.5 Παρελκόμενα που προορίζονται για χρήση σε συνδυασμό με το ιατροτεχνολογικό προϊόν**

Η μονάδα FemoSeal™ παρέχεται σε συσκευασία με έναν διαστολέα, οδηγό σύρμα 0,038” (0,97 mm) OD, μήκους 27,5” (70 cm) και εργαλείο ευθυγράμμισης σχήματος J. Το οδηγό σύρμα αποτελεί παρελκόμενο της μονάδας FemoSeal™. Η διάταξη ευθυγράμμισης σχήματος J αποτελεί εξάρτημα του οδηγού σύρματος, ενώ ο διαστολέας αποτελεί εξάρτημα της μονάδας FemoSeal™. Το οδηγό σύρμα είναι το μόνο εξάρτημα που θεωρείται παρελκόμενο. Το οδηγό σύρμα βρίσκεται μέσα σε έναν σωλήνα πολυαιθυλενίου. Όλα τα εξαρτήματα είναι συσκευασμένα σε έναν σταθερό χάρτινο δίσκο. Η συσκευασία περιλαμβάνει επίσης την κάρτα εμφυτεύματος ασθενούς. Το FemoSeal™ Vascular Closure System δεν απαιτεί τη χρήση πρόσθετων παρελκομένων προκειμένου το ιατροτεχνολογικό προϊόν να λειτουργεί όπως προορίζεται και το προϊόν

προορίζεται για χρήση μόνο με τον διαστολέα και το οδηγό σύρμα που περιλαμβάνονται στη συσκευασία του προϊόντος.

### 1.2.6 Άλλα ιατροτεχνολογικά προϊόντα και προϊόντα που προορίζονται για χρήση σε συνδυασμό με το ιατροτεχνολογικό προϊόν

Το FemoSeal™ VCS δεν απαιτεί τη χρήση πρόσθετων προϊόντων για να λειτουργεί όπως προορίζεται.

## 1.3 Κίνδυνοι και προειδοποιήσεις

### 1.3.1 Υπολειπόμενοι κίνδυνοι και ανεπιθύμητες ενέργειες

Γνωστά ή προβλέψιμα ανεπιθύμητα συμβάντα, βλάβες και επιπλοκές που σχετίζονται με τη χρήση του FemoSeal™ VCS ως αποτέλεσμα των υπολειπόμενων κινδύνων παρατίθενται στον **Πίνακα 1.2**. Το ποσοστό εμφάνισης βασίζεται σε μια ανάλυση της τεκμηρίωσης κινδύνου και υπολογίζεται με βάση τα δεδομένα παρακολούθησης μετά την κυκλοφορία του προϊόντος στην αγορά από την 1η Σεπτεμβρίου 2019 έως την 31η Αυγούστου 2024. Δεν υπάρχουν άγνωστοι υπολειπόμενοι κίνδυνοι για το FemoSeal™ VCS και όλοι οι ισχύοντες κίνδυνοι έχουν αντιμετωπιστεί μέσω των οδηγιών χρήσης και της διαδικασίας διαχείρισης κινδύνων.

**Πίνακας 1.2. Ανεπιθύμητα συμβάντα/ Επιπλοκές FemoSeal**

| Βλάβη                        | Συχνότητα εμφάνισης (%) | Παράγοντες μετριασμού                                                                                                                                                                                                                                       |
|------------------------------|-------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Αλλεργική αντίδραση          | 0,0000                  | Για τις ενέργειες και τα σχέδια που αποσκοπούν στην όσο το δυνατόν μεγαλύτερη μείωση του κινδύνου έχουν ληφθεί υπόψη τα χαρακτηριστικά σχεδιασμού του προϊόντος, οι κατευθυντήριες οδηγίες κατασκευής, η σήμανση του προϊόντος και η εκπαίδευση του ιατρού. |
| Ανεύρυσμα                    | 0,0000                  |                                                                                                                                                                                                                                                             |
| Αρτηριοφλεβικό συρίγγιο      | 0,0001                  |                                                                                                                                                                                                                                                             |
| Απώλεια αίματος / αιμορραγία | 0,0280                  |                                                                                                                                                                                                                                                             |
| Θάνατος                      | 0,0002                  |                                                                                                                                                                                                                                                             |
| Εκχύμωση                     | 0,0000                  |                                                                                                                                                                                                                                                             |
| Εμβολή                       | 0,0000                  |                                                                                                                                                                                                                                                             |
| Αντίδραση σε ξένο σώμα       | 0,0000                  |                                                                                                                                                                                                                                                             |
| Αιμάτωμα                     | 0,0027                  |                                                                                                                                                                                                                                                             |
| Αιμορραγία                   | 0,0001                  |                                                                                                                                                                                                                                                             |

| Βλάβη                                 | Συχνότητα εμφάνισης (%) | Παράγοντες μετριασμού |
|---------------------------------------|-------------------------|-----------------------|
| Μόλυνση                               | 0,0002                  |                       |
| Φλεγμονώδης αντίδραση                 | 0,0000                  |                       |
| Αιμωδία                               | 0,0000                  |                       |
| Πόνος                                 | 0,0000                  |                       |
| Δυσφορία ασθενούς                     | 0,0004                  |                       |
| Καθυστέρηση επέμβασης/ διαδικασίας    | 0,0065                  |                       |
| Ψευδοανεύρυσμα                        | 0,0004                  |                       |
| Οπισθοπεριτοναϊκή αιμορραγία          | 0,0002                  |                       |
| Σηψαιμία                              | 0,0000                  |                       |
| Θρομβοεμβολή                          | 0,0000                  |                       |
| Θρόμβωση                              | 0,0001                  |                       |
| Απόφραξη αγγείου/ ισχαιμία κάτω άκρου | 0,0002                  |                       |
| Διάτρηση αγγείου                      | 0,0000                  |                       |
| Διατομή/ ρήξη ιστού αγγείου           | 0,0003                  |                       |

### 1.3.2 Προειδοποιήσεις και προφυλάξεις

#### Προειδοποιήσεις

- Μη χρησιμοποιείτε το προϊόν εάν η συσκευασία έχει υποστεί φθορά ή ο στείρος φραγμός δεν είναι άθικτος.
- Να μη χρησιμοποιείται μετά την ημερομηνία λήξης – η απόδοση των βιοαποικοδομήσιμων εξαρτημάτων ενδέχεται να μην είναι επαρκής.
- Μη χρησιμοποιείτε το προϊόν, εάν οποιαδήποτε στοιχεία φαίνεται να έχουν υποστεί ζημιά ή να είναι ελαττωματικά με οποιονδήποτε τρόπο.
- Η χρήση του FemoSeal™ Vascular Closure System όταν ενδέχεται να έχει προκληθεί βακτηριακή επιμόλυνση του επεμβατικού θηκαριού ή του περιβάλλοντος ιστού, μπορεί να προκαλέσει μόλυνση.
- Εάν υπάρχει υποψία ότι το οπίσθιο αρτηριακό τοίχωμα έχει διατρηθεί ή έχουν γίνει περισσότερες από μία αρτηριακές διατρήσεις, μη βασίζεστε αποκλειστικά στο

FemoSeal™ Vascular Closure System για την επίτευξη αρτηριακής αιμόστασης.  
Εφαρμόστε πρόσθετη χειροκίνητη ή μηχανική συμπίεση.

6. Εάν το σημείο διάτρησης βρίσκεται στη διακλάδωση της μηριαίας αρτηρίας ή περιφερικά σε αυτήν, το FemoSeal™ Vascular Closure System δεν θα πρέπει να χρησιμοποιείται, λόγω του κινδύνου εσφαλμένης τοποθέτησης της εσωτερικής στεγανοποίησης. Αυτό το συμβάν μπορεί να οδηγήσει σε αιμορραγικές επιπλοκές ή/και διατάραξη της φυσιολογικής ροής του αίματος.
7. Εάν εξακολουθεί να παρατηρείται αρτηριακή αιμορραγία από το σημείο της τομής, μην κόβετε το πολύκλωνο υλικό μέχρι να επιτευχθεί αιμόσταση. Εάν δεν επιτευχθεί αιμόσταση, στερεώστε το πολύκλωνο υλικό με ένα αποστειρωμένο επίθεμα τραύματος και εφαρμόστε συμπληρωματική συμπίεση, μέχρι να επιτευχθεί αιμόσταση. Σε περίπτωση εμμένουσας αρτηριακής αιμορραγίας, ενδέχεται να παρουσιαστούν σημαντικές αιμορραγικές επιπλοκές, οι οποίες ενδέχεται να οδηγήσουν σε τραυματισμό ή τον θάνατο του ασθενούς.
8. Μη χρησιμοποιείτε το FemoSeal™ Vascular Closure System εάν το σημείο διάτρησης είναι κοντά στον βουβωνικό σύνδεσμο, καθώς αυτό μπορεί να οδηγήσει σε οπισθοπεριτοναϊκό αιμάτωμα.
9. Οι ασθενείς με υψηλότερο κίνδυνο αιμορραγίας ενδέχεται να παρουσιάσουν αυξημένη απώλεια αίματος, η οποία απαιτεί μετάγγιση.
10. Εάν ο εσωτερικός δίσκος αποσπαστεί, μπορεί δυνητικά να προκαλέσει θρομβωτικό ή/και εμβολικό συμβάν.

### Προφυλάξεις

1. Η διαδικασία έκπτυξης του FemoSeal™ Vascular Closure System θα πρέπει να πραγματοποιείται από ιατρούς με κατάλληλη εκπαίδευση στη χρήση του ιατροτεχνολογικού προϊόντος.
2. Εκτελέστε μια περιορισμένη μηριαία αγγειογραφία ή μια μηριαία διάτρηση με υπερηχογραφική καθοδήγηση πριν από την έκπτυξη του FemoSeal™ Vascular Closure System.
3. Διακόψτε τη διαδικασία στις εξής περιπτώσεις:
  - Διάμετρος αυλού κοινής μηριαίας αρτηρίας < 5 mm.
  - Παρουσία στένωσης ή/και σημαντικής πλάκας κοντά στο σημείο διάτρησης της κοινής μηριαίας αρτηρίας.
  - Η αρτηριακή διάτρηση βρίσκεται στη διακλάδωση της μηριαίας αρτηρίας ή περιφερικά αυτής.

- ο Παρουσία ανώμαλων διακλαδώσεων ή ανωμαλιών αγγείων κοντά στο σημείο διάτρησης της κοινής μηριαίας αρτηρίας.
- 4. Εάν υπάρχει αιμάτωμα, απαιτείται ιδιαίτερη προσοχή για τη σωστή εισαγωγή του θηκαριού περιβλήματος κώνου στην αρτηρία.
- 5. Εφαρμόζετε τεχνική διάτρησης μονού τοιχώματος. Μην τρυπάτε το οπίσθιο τοίχωμα της αρτηρίας.
- 6. Τηρείτε πάντοτε την τεχνική αποστείρωσης όταν χρησιμοποιείτε το FemoSeal™ Vascular Closure System.
- 7. Το FemoSeal™ Vascular Closure System προορίζεται για μία μόνο χρήση και δεν πρέπει να επαναποστειρώνεται ή να επαναχρησιμοποιείται με οποιονδήποτε τρόπο. Η μονάδα FemoSeal™ είναι σχεδιασμένη με τέτοιο τρόπο ώστε να μην μπορεί να επαναχρησιμοποιηθεί.
- 8. Εάν κατά την έκπτυξη της εσωτερικής στεγανοποίησης αισθανθείτε μη αναμενόμενη αντίσταση, διακόψτε τη διαδικασία.
- 9. Για τη σωστή έκπτυξη της εσωτερικής στεγανοποίησης, επανατοποθετήστε τον αντίχειρά σας έτσι ώστε το κουμπί να μπορεί να επανέλθει ελεύθερα.
- 10. Βεβαιωθείτε ότι το άκρο του θηκαριού περιβλήματος κώνου της μονάδας FemoSeal™ βρίσκεται κάτω από την επιφάνεια του δέρματος πριν από την έκπτυξη του εξωτερικού δίσκου ασφάλισης. Ο εξωτερικός δίσκος ασφάλισης μπορεί να εκπτυχθεί ακούσια πάνω από το επίπεδο του δέρματος σε ασθενείς με μικρή απόσταση μεταξύ της μηριαίας αρτηρίας και του επιπέδου του δέρματος.
- 11. Για τη σωστή έκπτυξη ενδέχεται να είναι απαραίτητη μια τομή στο δέρμα πριν από την έκπτυξη.
- 12. Εάν η εσωτερική στεγανοποίηση βρίσκεται εντός της αρτηρίας, αλλά δεν είναι δυνατό να πατηθεί πλήρως το κουμπί και να εκπτυχθεί ο εξωτερικός δίσκος ασφάλισης, ενδέχεται να απαιτείται χειρουργική επέμβαση για την αφαίρεση των στοιχείων του FemoSeal™ Closure.
- 13. Εάν απαιτείται νέα διάτρηση της ίδιας μηριαίας αρτηρίας εντός 18 μηνών, η νέα διάτρηση θα πρέπει να πραγματοποιηθεί τουλάχιστον ένα εκατοστό εγγύς της προηγούμενης θέσης πρόσβασης του FemoSeal™ Vascular Closure System.
- 14. Ζητήστε από τον ασθενή να ακολουθήσει τις οδηγίες του ιατρού σχετικά με τον έλεγχο του σημείου σύγκλεισης.
- 15. Ζητήστε από τον ασθενή να έχει μαζί του την Κάρτα πληροφοριών ασθενούς για τους επόμενους 18 μήνες

### **Προφυλάξεις κατά την έκδοση εξιτηρίου**

Πριν εξετάσετε το ενδεχόμενο έκδοσης εξιτηρίου, αξιολογήστε τον ασθενή για τις ακόλουθες κλινικές καταστάσεις:

1. Αιμορραγία ή/και αιμάτωμα στο σημείο σύγκλεισης.
2. Πόνος κατά το περπάτημα.
3. Ενδείξεις μόλυνσης στο σημείο σύγκλεισης.

### **1.3.3 Διορθωτικά μέτρα ασφαλείας κατά τη χρήση**

Εφαρμόστηκε μία Επιτόπια διορθωτική ενέργεια ασφάλειας σχετικά με το FemoSeal™ VCS στο χρονικό διάστημα από την 1η Σεπτεμβρίου 2019 έως την 31η Αυγούστου 2024.

Το 2022, η Terumo προέβη σε εθελοντική ανάκληση του FemoSeal™ VCS λόγω καταγγελιών σχετικά με αποτυχίες στη διαδικασία και τη δοκιμή αποδέσμευσης παρτίδας του προϊόντος FemoSeal που κατασκευάστηκε από την Elkton για τη μέτρηση της δύναμης συμπίεσης και της δύναμης συστολής. Συνολικά ανακλήθηκαν 950 μονάδες από τη Νότια Κορέα.

### **1.4 Κλινική αξιολόγηση και κλινική παρακολούθηση μετά την κυκλοφορία του προϊόντος στην αγορά**

Στον **Πίνακα 1.3** περιλαμβάνεται ένας κατάλογος βασικών μελετών που περιλήφθηκαν για τη διάθεση του FemoSeal™ VCS στην αγορά καθώς και μελετών μετά την κυκλοφορία του προϊόντος στην αγορά και δραστηριοτήτων κλινικής παρακολούθησης μετά την κυκλοφορία του προϊόντος στην αγορά. Η έκδοση του ιατροτεχνολογικού προϊόντος που χρησιμοποιείται στη μελέτη περιλαμβάνεται στον παρακάτω πίνακα. Η πρώτη έκδοση του FemoSeal™ VCS (αριθ. 11200) διατέθηκε στην αγορά μέχρι το 2006, ενώ η επόμενη έκδοση (αριθ. C11202) διατέθηκε στην αγορά το 2006 και είναι η τρέχουσα έκδοση που διατίθεται στην αγορά σήμερα.

**Πίνακας 1.3 Σύνοψη βασικών μελετών**

| Λειτουργικές δοκιμές σε ζώα πριν από την κυκλοφορία του προϊόντος στην αγορά                                                                                                                                                                                            | Έκδοση ιατροτεχνολογικού προϊόντος |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                              |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                              |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                              |

|                                                                                                                                                                                                              |                                         |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| Πρώτη κλινική μελέτη σε ανθρώπους                                                                                                                                                                            |                                         |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 11200                                   |
| Ολοκληρωμένες κλινικές μελέτες μετά την κυκλοφορία του προϊόντος στην αγορά                                                                                                                                  |                                         |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                   | C11202 (τρέχον ιατροτεχνολογικό προϊόν) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                            | C11202 (τρέχον ιατροτεχνολογικό προϊόν) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                                                                                               | C11202 (τρέχον ιατροτεχνολογικό προϊόν) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)                                                                                       | C11202 (τρέχον ιατροτεχνολογικό προϊόν) |
| Προγραμματισμένες/ συνεχιζόμενες κλινικές μελέτες μετά την κυκλοφορία του προϊόντος στην αγορά                                                                                                               |                                         |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                                                                                                   | C11202 (τρέχον ιατροτεχνολογικό προϊόν) |
| Δραστηριότητες κλινικής παρακολούθησης μετά την κυκλοφορία του προϊόντος στην αγορά                                                                                                                          |                                         |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                                                                                                    | C11202 (τρέχον ιατροτεχνολογικό προϊόν) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                                                                                                           | C11202 (τρέχον ιατροτεχνολογικό προϊόν) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024)                                                                              | C11202 (τρέχον ιατροτεχνολογικό προϊόν) |

**1.4.1 Σύνοψη δεδομένων για το διάστημα πριν από την κυκλοφορία του προϊόντος στην αγορά (από δοκιμές σε ζώα και κλινικές έρευνες)**

Στον **Πίνακα 1.4** παρακάτω περιγράφονται όλες οι μελέτες πριν από την κυκλοφορία του προϊόντος στην αγορά, είτε πρόκειται για δοκιμές σε ζώα είτε για κλινικές έρευνες.



**Πίνακας 1.4 Συνόψεις μελετών πριν από την κυκλοφορία του προϊόντος στην αγορά**

| Λειτουργικές δοκιμές σε ζώα πριν από την κυκλοφορία του προϊόντος στην αγορά                                                                                                                                                                                            |                                                                          |                                             |                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|---------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Όνομα μελέτης                                                                                                                                                                                                                                                           | Ετος / CI                                                                | Τύπος μελέτης                               | Στόχοι                                                                                                                                                                                                                                                                                    | Ορόσημα                                                                                                                                                                                                                                                                                                                                                                               | Πιθανά κριτήρια αποδοχής                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 2000<br>Radi Medical System AB<br><br>Διεξήχθη από την Biomatech, Γαλλία | Μελέτη σε πειραματόζωα, διερευνητική έρευνα | Στόχος της μελέτης ήταν η αξιολόγηση της βιοσυμβατότητας και της βιολειτουργικότητας ενός βιοαποικοδομήσιμου εμφυτεύματος, σχεδιασμένου για την επίτευξη αιμόστασης στο αγγειακό σύστημα. Η έκθεση αναφέρεται σε εφεδρικά πειραματόζωα από τη Μελέτη με αριθμό 862 (Αρ. εγγράφου 1051-01) | N = 3 ενήλικα θηλυκά πρόβατα, 1 πειραματόζωο ανά χρονικό σημείο<br><br>Παρακολούθηση για ιστοπαθολογική ανάλυση, μακροσκοπική διαβάθμιση και υπερδομική ανάλυση<br><br><ul style="list-style-type: none"> <li>12 μήνες</li> <li>15 μήνες</li> <li>18 μήνες</li> </ul><br>Παρακολούθηση με υπερήχους έγχρωμου doppler – 30 ημέρες στα σημεία πρόσβασης καρωτίδας και μηριαίας αρτηρίας | Αρτηριακή βατότητα <ul style="list-style-type: none"> <li>Αξιολόγηση ροής αίματος μετά την έκπτυξη – μείωση της ροής αίματος κατά 2/3 που συσχετίζεται με προσωρινό αρτηριακό αγγειόσπασμο που αποδόθηκε στην επέμβαση, και με τα δύο συμβάντα να παρουσιάζονται στην αριστερή κοινή καρωτιδική αρτηρία</li> <li>Αξιολόγηση με υπερήχους έγχρωμου doppler (4 εβδομάδες) – 3/3 (100%) χωρίς μεγάλη μείωση της ροής του αίματος 30 ημέρες μετά την εμφύτευση</li> </ul><br>Μακροσκοπικές παρατηρήσεις <ul style="list-style-type: none"> <li>12 μήνες – η βατότητα επιβεβαιώθηκε μακροσκοπικά, με απουσία ανατομικά ορατής απόφραξης. Δεν εμφανίστηκαν βλάβες μακροσκοπικής τοπικής δυσανεξίας (αιμορραγία, νέκρωση ή νεοαγγείωση). Η ενθυλάκωση του εσωτερικού δίσκου φαίνεται να επισημαίνεται</li> <li>15 μήνες - η μακροσκοπική παρατήρηση δεν ανέδειξε ενδείξεις φλεγμονής. Δεν εντοπίστηκαν υπολείμματα εσωτερικών ή εξωτερικών δίσκων. Ο ιστός ενθυλάκωσης που βρίσκεται στην περιοχή του εξωτερικού δίσκου εμφανίστηκε όμοιος με την παρατήρηση στους 12 μήνες</li> <li>18 μήνες – η μακροσκοπική παρατήρηση δεν</li> </ul> |



|                                                                                                                                                                                                                 |                                                                              |                                                    |                                                                                                                                                                      |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
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|                                                                                                                                                                                                                 |                                                                              |                                                    |                                                                                                                                                                      |                                                                                                                                                                                                                           | <p>ανέδειξε ενδείξεις τοπικής δυσανεξίας. Ο εξωτερικός δίσκος είναι ορατός (3/3 περιστατικά), η αποδόμηση του εσωτερικού δίσκου ολοκληρώθηκε. 1/3 (αριστερή κοινή καρωτίδα αρτηρία) - παρατηρείται συμπίεση του αρτηριακού τοιχώματος στο σημείο του εμφυτεύματος (μπορεί να συσχετίζεται με την έκπτυξη του ιατροτεχνολογικού προϊόντος)</p> <p>Συμπεράσματα</p> <ul style="list-style-type: none"> <li>Μακροσκοπικά, 12, 15 και 18 μήνες μετά την εμφύτευση, δεν εντοπίστηκαν νεκρωτικές, εκφυλιστικές ή θρομβωτικές ενδείξεις.</li> <li>Η διαδικασία αποδόμησης των εσωτερικών και εξωτερικών δίσκων φαίνεται να εξελίσσεται μεταξύ 12 και 18 μηνών και να ολοκληρώνεται στους 18 μήνες, με έναν λευκωπό ιστό να καλύπτει την περιοχή του εμφυτεύματος.</li> <li>Ιστολογικά, μετά από 18 μήνες, το πολυμερές υλικό δεν ήταν πλέον ορατό, αλλά υπήρχε παρουσία ενδοαυλικού ινώδους ιστού. Δεν παρατηρήθηκαν νεκρωτικές, εκφυλιστικές ή θρομβωτικές βλάβες.</li> </ul> |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1),</p> | <p>2002 Radi Medical System AB</p> <p>Διεξήχθη από την Biomatech, Γαλλία</p> | <p>Μελέτη σε πειραματόζωα, διερευνητική έρευνα</p> | <p>Στόχος της μελέτης ήταν η αξιολόγηση της βιοσυμβατότητας ενός βιοαποικοδομήσιμου εμφυτεύματος, σχεδιασμένου για την επίτευξη αιμόστασης στο αγγειακό σύστημα.</p> | <p>Παρακολούθηση (μετά την εμφύτευση)</p> <ul style="list-style-type: none"> <li>12 εβδομάδες</li> <li>24 εβδομάδες</li> <li>36 εβδομάδες</li> </ul> <p>N = 12 πρόβατα, 3 πειραματόζωα ανά χρονικό σημείο, 3 εφεδρικά</p> | <p><u>Βατότητα καρωτιδικών και μηριαίων αρτηριών μετά από 4 εβδομάδες</u></p> <ul style="list-style-type: none"> <li>Σημαντική μείωση της αιματικής ροής 0/12 (0%)</li> </ul> <p><u>Καμία σημαντική μείωση της αιματικής ροής</u></p> <ul style="list-style-type: none"> <li>Βαριάς μορφής διαταραχή της ροής του</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |

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| 2002, Radi Medical System AB (performed by Biomatech, France). |  |  |  | <p>πειραματόζωα στους 12, 15 και 18 μήνες</p> <p>Σημεία εμφύτευσης – αριστερή και δεξιά μηριαία αρτηρία, δεξιά και αριστερή κοινή καρωτιδική αρτηρία</p> <p>Ανάλυση υπερήχων έγχρωμου doppler</p> | <p>αίματος που σχετίζεται με την εισαγωγή του ιατροτεχνολογικού προϊόντος 0/12 (0%)</p> <ul style="list-style-type: none"> <li>Μείωση της ροής αίματος στην αριστερή κοινή καρωτίδα 2/12 (16,6%) λόγω προσωρινού αρτηριακού αγγειοσπασμού (που σχετίζεται με τη χειρουργική επέμβαση, όχι με το ιατροτεχνολογικό προϊόν)</li> </ul> <p><u>Διαταραχή αιματικής ροής κατά την παρακολούθηση</u></p> <p>12 εβδομάδες – 0/12 (0%)</p> <p>24 εβδομάδες – 0/12 (0%)</p> <p>36 εβδομάδες – 0/12 (0%)</p> <p>Μετρήσεις αρτηριακής πίεσης (3 πρόβατα – 36 εβδομάδες)</p> <ul style="list-style-type: none"> <li>Δεν ανιχνεύθηκε σημαντική μείωση ροής αίματος</li> </ul> <p>Μακροσκοπικά δεδομένα για ενσωμάτωση και αποδόμηση (Βαθμίδα 0-4)</p> <p><u>Καρωτιδικά σημεία</u></p> <p><u>Εσωτερική πλευρά</u></p> <p>-ενθulάκωση</p> <p>12 εβδομάδες 1,3</p> <p>24 εβδομάδες 0,8</p> <p>36 εβδομάδες 0,7</p> <p>-αποδόμηση υλικού</p> <p>12 εβδομάδες 2,2</p> <p>24 εβδομάδες 2,3</p> <p>36 εβδομάδες 0,7</p> <p><u>Εξωτερική πλευρά</u></p> <p>-ενθulάκωση</p> <p>12 εβδομάδες 2,0</p> <p>24 εβδομάδες 1,0</p> <p>36 εβδομάδες 0,8</p> <p>-αποδόμηση υλικού</p> <p>12 εβδομάδες 2,0</p> <p>24 εβδομάδες 2,7</p> <p>36 εβδομάδες 3,2</p> |
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|  |  |  |  |  | <p><u>Μηριαία σημεία</u></p> <p>Εξωτερική πλευρά</p> <p>-ενθυλάκωση</p> <p>12 εβδομάδες 1,0</p> <p>24 εβδομάδες 2,7</p> <p>36 εβδομάδες 1,0</p> <p>-αποδόμηση υλικού</p> <p>12 εβδομάδες 2,0</p> <p>24 εβδομάδες 2,4</p> <p>36 εβδομάδες 3,0</p><br><p>Εσωτερική πλευρά</p> <p>-ενθυλάκωση</p> <p>12 εβδομάδες 2,0</p> <p>24 εβδομάδες 1,2</p> <p>36 εβδομάδες 1,0</p> <p>-αποδόμηση υλικού</p> <p>12 εβδομάδες 1,0</p> <p>24 εβδομάδες 2,2</p> <p>36 εβδομάδες 3,0</p><br><p><u>Ιστολογικά δεδομένα για παράγοντες ενσωμάτωσης, αποδόμησης και φλεγμονής (μέση τιμή σχετικών τιμών, Δείκτης 0-4) n=6</u></p><br><p><u>Καρωτιδικά σημεία</u></p> <p>Εξωτερική ίνωση</p> <p>12 εβδομάδες – 2,3</p> <p>24 εβδομάδες – 2,3</p> <p>36 εβδομάδες – 1,8</p> <p>Εσωτερικός νεοχιτώνας</p> <p>12 εβδομάδες – 3,0</p> <p>24 εβδομάδες – 2,7</p> <p>36 εβδομάδες – 3,3</p> <p>Αποδόμηση υλικού</p> <p>12 εβδομάδες – 1,7</p> <p>24 εβδομάδες – 3,0</p> <p>36 εβδομάδες – 3 +</p> <p>Φλεγμονώδεις παράμετροι (μακροφάγα)</p> <p>12 εβδομάδες – 3,0</p> <p>24 εβδομάδες – 1,7</p> <p>36 εβδομάδες – 1,7</p> <p><u>Μηριαία σημεία</u></p> <p>Εξωτερική ίνωση</p> <p>12 εβδομάδες – 1,3</p> <p>24 εβδομάδες – 1,5</p> <p>36 εβδομάδες – 1,7</p> <p>Εσωτερικός νεοχιτώνας</p> |
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|  |  |  |  |  | <div> <div> 12 εβδομάδες – 3,7<br/> 24 εβδομάδες – 3,3<br/> 36 εβδομάδες – 3,8<br/> Αποδόμηση υλικού<br/> 12 εβδομάδες – 2,0<br/> 24 εβδομάδες – 3,0<br/> 36 εβδομάδες – 3+<br/> Φλεγμονώδεις παράμετροι (μακροφάγα)<br/> 12 εβδομάδες – 3,5<br/> 24 εβδομάδες – 1,8<br/> 36 εβδομάδες – 1,8 </div> <div> <u>Τιμές ιστομορφολογικής βατότητας</u><br/> Καρωτιδικά σημεία<br/> 12 εβδομάδες 74,0%<br/> 24 εβδομάδες 81,9%<br/> 36 εβδομάδες -89,43%<br/> Μηριαία σημεία<br/> 12 εβδομάδες – 42,2%<br/> 24 εβδομάδες – 73,21%<br/> 36 εβδομάδες – 78,71% </div> <div> <u>Βατότητα αγγείων US (μέση τιμή %)</u><br/> Καρωτιδικό σημείο<br/> 12 εβδομάδες 94,6%<br/> 24 εβδομάδες – 96,7%<br/> 36 εβδομάδες – 94,7%<br/> Μηριαία σημεία<br/> 12 εβδομάδες – 66,9%<br/> 24 εβδομάδες – 63,6%<br/> 36 εβδομάδες – 75,1% </div> <div> <u>Συμπεράσματα</u><br/> <ul style="list-style-type: none"> <li>Δεν ανιχνεύθηκε σημαντική τοπική δυσανεξία (εμφάνιση ορατών φλεγμονωδών, νεκρωτικών ή εκφυλιστικών βλαβών) στις 12, 24 ή 36 εβδομάδες</li> <li>Δεν καταγράφηκαν σημαντικές ανεπιθύμητες αντιδράσεις ιστού σε σχέση με τον ξενιστή και το ιατροτεχνολογικό προϊόν</li> <li>Η αποδόμηση του εμφυτεύματος ολοκληρώθηκε σχεδόν</li> </ul> </div> </div> |
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| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France). | 2002<br><br>Radi Medical System AB<br><br>Διεξήχθη από την Biomatech, Γαλλία | Μελέτη σε ζώα | Σκοπός της μελέτης ήταν η αξιολόγηση της βιοσυμβατότητας και της βιολειτουργικότητας ενός βιοαποικοδομήσιμου εμφυτεύματος, σχεδιασμένου για την επίτευξη αιμόστασης στο αγγειακό σύστημα. Το ιατροτεχνολογικό προϊόν που ελέγχθηκε προορίζεται να εισέλθει στην οπή διάτρησης σε αρτηρίες για την επίτευξη αιμόστασης. Ο ένας δίσκος εισήλθε στην οπή διάτρησης της αρτηρίας και ο άλλος συμπίεσε τον εσωτερικό δίσκο από το εξωτερικό της αρτηρίας. Και οι δύο δίσκοι εισήχθησαν μέσω ενός θηκαριού εισαγωγής. Οι δίσκοι σχεδιάστηκαν για να αποτρέπουν την αιμορραγία, να επουλώνονται στο τοίχωμα του αγγείου και τελικά να αποδομούνται και να απορροφούνται. Η μελέτη σχεδιάστηκε για τη συλλογή και την ανάλυση δεδομένων μετά από λειτουργική εμφύτευση σε προβατοειδή και χοίρους, για την αξιολόγηση της ικανότητας του εμφυτεύματος να διατηρεί φυσιολογική λειτουργία, όταν χρησιμοποιείται στο κυκλοφορικό σύστημα, για τον προσδιορισμό της απόκρισης του ξενιστή και της απόκρισης του ιατροτεχνολογικού προϊόντος (φυσική ακεραιότητα, ενθυλάκωση | Η περίοδος εμφύτευσης/ παρακολούθησης είναι 5 εβδομάδες για όλα τα πειραματόζωα<br><br>4 πρόβατα, 1 χοίρος<br><br>14 στοιχεία σύγκλεισης<br><br>8 στοιχεία σύγκλεισης εμφυτευμένα σε 2 πρόβατα,<br><br>2 στοιχεία σύγκλεισης εμφυτευμένα σε 1 χοίρο<br><br>Όταν εμφυτεύθηκαν δύο στοιχεία σύγκλεισης στην ίδια μηριαία αρτηρία, εμφυτεύθηκαν σε απόσταση > 30 mm | Καταγράφηκαν κριτήρια τυχόν ανεπιθύμητων συμβάντων (φλεγμονή, νέκρωση, αιμορραγία ή οποιαδήποτε άλλη βλάβη) ή τυχόν σχηματισμός λεπτού ψευδο-εσωχιτώνιου στρώματος. Ιδιαίτερη προσοχή δόθηκε στην αρχική ενσωμάτωση του ιατροτεχνολογικού προϊόντος στον ιστό, με έμφαση στην ενθυλάκωση του εσωτερικού δίσκου.<br><br>Μακροσκοπικά, δεν παρατηρήθηκαν σημαντικές ενδείξεις τοπικής δυσανεξίας ή σχηματισμού θρόμβου. Η μακροσκοπική παρατήρηση δεν αποκάλυψε καμία διαφορά μεταξύ του προβάτου ή του χοίρου μετά την εμφύτευση των στοιχείων σύγκλεισης στις μηριαίες αρτηρίες. Μακροσκοπικά, δεν παρατηρήθηκαν σημαντικές ενδείξεις τοπικής δυσανεξίας ή σχηματισμού θρόμβου. Η μακροσκοπική παρατήρηση δεν αποκάλυψε καμία διαφορά μεταξύ του προβάτου ή του χοίρου μετά την εμφύτευση των στοιχείων σύγκλεισης στις μηριαίες αρτηρίες.<br><br>Η ιστολογική ανάλυση της θέσης εμφύτευσης σε πρόβατα δεν έδειξε τοπικές ανεπιθύμητες αντιδράσεις. Οι |

|  |  |  | ιστού) και για την αξιολόγηση της αποδόμησης του εμφυτεύματος |  | <p>εσωτερικοί και εξωτερικοί δίσκοι παρουσίασαν ενδείξεις αποδόμησης και σε ορισμένες περιπτώσεις διασπάστηκαν σε μικρότερα μέρη. Οι εσωτερικοί δίσκοι ενσωματώθηκαν πλήρως στον νεο-εσωχιτώνιο ιστό. Στον χοίρο, η ιστολογική ανάλυση αποκάλυψε ελαφρώς περισσότερες φλεγμονώδεις ενδείξεις γύρω από τους εσωτερικούς και εξωτερικούς δίσκους. Και στα δύο πειραματόζωα, το πολυκύκλωνο παρουσίασε ελαφρώς περισσότερες φλεγμονώδεις ενδείξεις σε σχέση με το υλικό του δίσκου, γεγονός φυσιολογικό για τα πλεκτά ράμματα, λόγω της μεγαλύτερης επιφάνειας.</p> <p>Η βατότητα των αγγείων μετρήθηκε μετά από 5 εβδομάδες με χρήση τριών διαφορετικών μεθόδων - ιστομορφομετρική, ιστομορφομετρική σε συνδυασμό με μέτρηση της διαμέτρου του αγγείου με χρήση παχύμετρου και με χρήση υπερηχογραφήματος έγχρωμου doppler. Η μέση βατότητα των αγγείων στα πρόβατα ήταν μεταξύ 60 και 80%, ανάλογα με τη μέθοδο (12 παρατηρήσεις). Στον χοίρο, η μέση βατότητα στο αγγείο ήταν μεταξύ 40% και 80% (2 παρατηρήσεις).</p> |
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| Πρώτη κλινική μελέτη σε ανθρώπους                                                                                                                                                                            |                              |                                                       |                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Όνομα μελέτης                                                                                                                                                                                                | Έτος / CI                    | Τύπος μελέτης                                         | Στόχοι                                                                                                                                                                                                                                                                                                                                     | Ορόσημα                                                                                                                                                                                                                                                                                                                                                     | Πιθανά κριτήρια αποδοχής                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Δοκιμή ανοικτής ετικέτας, μονού σκέλους, πολυκεντρική | Στόχοι της μελέτης ήταν ο καθορισμός της ασφάλειας, της απόδοσης και της αποτελεσματικότητας του Συστήματος σύγκλεισης αγγείων FemoSeal (Σύστημα FemoSeal) γενικά, και συγκεκριμένα των στοιχείων σύγκλεισης, σε ασθενείς που υποβάλλονται σε διαγνωστικές ή επεμβατικές καρδιολογικές διαδικασίες με χρήση πρόσβασης στη μηριαία αρτηρία. | Μελέτη 2 μερών<br>Συνολικό n = 80<br>Μέρος 1 n = 20<br>Μέρος 2 n = 60<br>Ενδείξεις:<br>Μέρος 1 – διαγνωστικός καρδιακός καθετηριασμός με χρήση μηριαίας αρτηρίας ως σημείο πρόσβασης<br>Μέρος 2 – ασθενείς που υποβάλλονται σε διαγνωστικές και επεμβατικές καρδιακές διαδικασίες με χρήση μηριαίας αρτηρίας ως σημείο πρόσβασης<br>Παρακολούθηση 30 ημερών | Αποτελέσματα<br>- <u>επίτευξη αιμόστασης με συγκολλητικό από ινώδες, χωρίς συμπίεση</u><br>- Μέρος 1 20/20 (100%)<br>- Μέρος 2 58/60 (97%)<br>Διάμεσος χρόνος έως την αιμόσταση κατά τον χρόνο της επέμβασης/διαδικασίας (μέρος 2) – 1,0 λεπτό (Άμεσο εύρος – 8 λεπτά)<br><u>Χρόνος έως το περιπατητικό στάδιο (λεπτά)</u><br>Μέρος 1 –<br>Διάμεση τιμή: 33,0<br>Μέση τιμή: 67,8<br>Μέρος 2 –<br>Διάμεση τιμή: 45<br>Μέση τιμή: 87,5<br><u>Επιπολασμός σοβαρών αγγειακών επιπλοκών – παρακολούθηση 30 ημερών</u><br>Μέρος 1<br>- Χωρίς αγγειακές επιπλοκές 20/20 (100%)<br>Μέρος 2<br>Ψευδοανεύρυσμα - 1/59 (1,69%)<br><u>Αποτυχία θεραπείας</u><br>Μέρος 1 – 0/20 (0%)<br>Μέρος 2 – 3/60 (5%)<br>• 2 λόγω αδυναμίας επίτευξης αιμόστασης χωρίς χρήση συμπίεσης |

|  |  |  |  |  | <ul style="list-style-type: none"> <li>1 λόγω σοβαρής αγγειακής επιπλοκής, ψευδοανεύρυσμα</li> </ul> <p><u>Επιμέλλον έκκριμα</u><br/>Μέρος 1 – 0/20 (0%)<br/>Μέρος 2 – 8/60 (13%)</p> <p><u>Αιμάτωμα</u><br/>Μέρος 1 – 0/20 (0%)<br/>Μέρος 2 – 6/60 (10%)</p> |
|--|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Στο πλαίσιο του σχεδίου ανάπτυξης πριν από τη διάθεση στην αγορά για το FemoSeal™ VCS, ολοκληρώθηκαν 3 λειτουργικές δοκιμές σε πειραματόζωα. Το 2000, πριν από την έναρξη κλινικών μελετών, πραγματοποιήθηκε μια μελέτη σε πειραματόζωα για την αξιολόγηση της βιολειτουργικότητας του FemoSeal™ VCS. Η μελέτη αυτή αξιολόγησε την ικανότητα των στοιχείων σύγκλεισης στη διατήρηση της φυσιολογικής λειτουργίας και την αποδόμησή τους. Στους 18 μήνες, το υλικό του εσωτερικού και του εξωτερικού δίσκου δεν ήταν πλέον ορατό, έχοντας αντικατασταθεί από έναν ενδοαυλικό ινώδη ιστό. Συμπερασματικά, επιβεβαιώθηκε η δυνατότητα του στοιχείου σύγκλεισης του FemoSeal™ VCS να διατηρεί τη φυσιολογική λειτουργία, όταν χρησιμοποιείται στο κυκλοφορικό σύστημα.

Το 2002 πραγματοποιήθηκε μελέτη σε πειραματόζωα για την αξιολόγηση της βιοσυμβατότητας ενός βιοαποικοδομήσιμου εμφυτεύματος, του FemoSeal™ VCS, σχεδιασμένου για την επίτευξη αιμόστασης στο αγγειακό σύστημα. Περιληπτικά, η αποδόμηση του εμφυτεύματος είχε σχεδόν ολοκληρωθεί έως τις 36 εβδομάδες και δεν παρατηρήθηκε σημαντική ανεπιθύμητη αντίδραση στον ιστό.

Μια άλλη μελέτη σε πειραματόζωα το 2002 αξιολόγησε τη βιοσυμβατότητα και τη βιολειτουργικότητα ενός βιοαποικοδομήσιμου εμφυτεύματος, του FemoSeal™ VCS, σχεδιασμένου για την επίτευξη αιμόστασης στο αγγειακό σύστημα. Μετά από 5 εβδομάδες, η ενθυλάκωση του δίσκου είχε ολοκληρωθεί και παρατηρήθηκαν ενδείξεις αποδόμησης των εσωτερικών και εξωτερικών δίσκων. Συμπερασματικά, επιβεβαιώθηκε η δυνατότητα του εμφυτεύματος να διατηρεί τη φυσιολογική λειτουργία, όταν χρησιμοποιείται στο κυκλοφορικό σύστημα.

Στο πλαίσιο του σχεδίου κλινικής ανάπτυξης για το FemoSeal™ VCS, η Radi Medical System AB διεξήγαγε μια κλινική έρευνα πριν από τη διάθεση στην αγορά. Αυτή η κλινική έρευνα δεν δημοσιεύτηκε ή δεν είναι διαθέσιμη ηλεκτρονικά. Η μελέτη με το μοντέλο ιατροτεχνολογικού



προϊόντος #11200 πραγματοποιήθηκε το 2002-2004 στο πλαίσιο του Ευρωπαϊκού Προτύπου EN 540 (Κλινική Διερεύνηση Ιατροτεχνολογικών Προϊόντων για Ανθρώπους) και σύμφωνα με τα Γενικά Ζητήματα ICH για τις Κλινικές Δοκιμές και την Οδηγία για την Ορθή Κλινική Πρακτική. Οι λεπτομέρειες αυτής της μελέτης τεκμηριώνονται στην έκθεση EU-SE-001. Η κλινική δοκιμή καταγράφηκε στην Τελική Έκθεση από τη Radi Medical Systems AB, «Πολυκεντρική κλινική δοκιμή του Συστήματος σύγκλεισης αγγείων FemoSeal για τη στεγανοποίηση των διατρήσεων μηριαίων αρτηριών μετά από διαγνωστικές/ επεμβατικές καρδιολογικές διαδικασίες». Η κλινική μελέτη πραγματοποιήθηκε με το πρώτο μοντέλο αριθ. 11200 του FemoSeal™ και εστίασε στην ασφάλεια και την αποτελεσματικότητα των εμφυτεύσιμων στοιχείων σύγκλεισης. Η μόνη διαφορά μεταξύ του πρώτου μοντέλου αριθ. 11200 και του τρέχοντος μοντέλου, C11202, είναι το μέγεθος French, 6F και 7F αντίστοιχα, και το βελτιωμένο σύστημα χορήγησης. Τα κλινικά οφέλη, η προβλεπόμενη χρήση, οι αρχές λειτουργίας και οι πρώτες ύλες των εμφυτεύσιμων στοιχείων σύγκλεισης, της εσωτερικής στεγανοποίησης και του εξωτερικού δίσκου ασφάλισης παραμένουν αμετάβλητα.

Η προβλεπόμενη χρήση του ιατροτεχνολογικού προϊόντος αφορούσε ασθενείς που υποβλήθηκαν σε διαγνωστικές ή επεμβατικές καρδιακές διαδικασίες/ επεμβάσεις με χρήση της μηριαίας αρτηρίας ως σημείο πρόσβασης. Στόχος της παρούσας μελέτης ήταν ο καθορισμός της ασφάλειας, της απόδοσης και της αποτελεσματικότητας του FemoSeal™ VCS. Η μελέτη ήταν μια προοπτική, πολυκεντρική μελέτη, ανοικτής ετικέτας, ενός σκέλους, με παρακολούθηση 30 ημερών.

Το πρωτεύον τελικό σημείο απόδοσης ήταν ο χρόνος έως την επίτευξη αιμόστασης που ορίστηκε ως η απουσία έντονης αιμορραγίας. Το πρωτεύον τελικό σημείο ασφάλειας ήταν η εμφάνιση σοβαρών αγγειακών επιπλοκών έως και 30 ημέρες αργότερα. Στα δευτερεύοντα τελικά σημεία περιλαμβάνονταν ο χρόνος έως το περιπατητικό στάδιο, το ποσοστό αποτυχιών θεραπείας, ο επιπολασμός των ανεπιθύμητων συμβάντων και τα χαρακτηριστικά απόδοσης του ιατροτεχνολογικού προϊόντος κατά τη διάρκεια της χορήγησης και της έκπτυξης.

Οι ασθενείς που συμπεριλήφθηκαν σε αυτήν τη μελέτη ήταν ενήλικες που μπόρεσαν να παράσχουν συναίνεση κατόπιν ενημέρωσης και με τουλάχιστον έναν ακέραιο πελματιαίο σφυγμό. Οι ασθενείς αποκλείστηκαν από τη μελέτη εάν είχαν κάποια από τις ακόλουθες καταστάσεις:

- Ιστορικό περιφερικής αγγειακής νόσου
- Αυτοάνοσο νόσημα
- Γνωστή αιμορραγική διαταραχή βαριάς αναιμίας
- INR > 1,5
- Έμφραγμα του μυοκαρδίου εντός 72 ωρών

- Μη ελεγχόμενη υπέρταση παρά τη θεραπεία
- Παχυσαρκία που αποκλείει την πρόσβαση με τεχνική Seldinger
- Παρουσία αγγειακού μοσχεύματος ή ενδοπρόθεσης στο σημείο της αρτηριοτομής
- Προηγούμενη ομόπλευρη διάτρηση εντός 3 μηνών
- Προσδόκιμο ζωής < 6 μήνες

Επιπλέον, οι ασθενείς εξετάστηκαν ενδοεγχειρητικά και αποκλείστηκαν από τη μελέτη εάν παρατηρήθηκε οποιοδήποτε από τα ακόλουθα:

- Διάμετρος αυλού κοινής μηριαίας αρτηρίας < 5 mm
- Αρτηριακές διακλαδώσεις σε απόσταση 2 cm εγγύς του σημείου διάτρησης
- Σημαντική στένωση εντός 3 cm από το σημείο διάτρησης
- Χρήση του κύριου θηκαριού εισαγωγέα > 6 Fr
- Διάτρηση στο σημείο της μηριαίας διακλάδωσης ή περιφερικά αυτού
- Πολλαπλές μηριαίες διατρήσεις
- Γνωστή ή πιθανολογούμενη διάτρηση του οπίσθιου μηριαίου τοιχώματος
- Μεγάλο αιμάτωμα (2:6 cm) κατά την ολοκλήρωση της επέμβασης
- Δυσκολία εισαγωγής του πρωτεύοντος θηκαριού για την επέμβαση λόγω δυσχερούς ιστού ή αγγείου

Αυτή η μελέτη μονού πρωτοκόλλου πραγματοποιήθηκε σε δύο μέρη: Στη διάρκεια του Μέρους 1 εντάχθηκαν 20 ασθενείς. Ολοκληρώθηκε μια ανάλυση ασφάλειας και, στη συνέχεια, εντάχθηκαν επιπλέον 60 ασθενείς κατά το Μέρος 2.

Στο Μέρος 1, η μέση ηλικία των ενταγμένων ασθενών ήταν 65,9 έτη, το 70,0% των ασθενών ήταν άνδρες και το 95% των ασθενών λάμβανε συγχρησιμοποιούμενα φάρμακα. Στο Μέρος 2 της μελέτης, η μέση ηλικία ήταν 63,8 έτη, το 78% ήταν άντρες και το 100% λάμβανε συγχρησιμοποιούμενα φάρμακα.

Οι ασθενείς που υποβλήθηκαν σε διαγνωστικές (Μέρος 1 και Μέρος 2) ή επεμβατικές (Μέρος 2) διαδικασίες καρδιακού καθετηριασμού ήταν επιλέξιμοι για συμμετοχή στη μελέτη. Οι διαδικασίες ήταν σύμφωνες με την καθιερωμένη θεραπεία σε καθένα από τα εγχευόμενα νοσοκομεία, ενώ ακολούθησε η χρήση του FemoSeal™ VCS. Τα δεδομένα ασθενών συλλέχθηκαν κατά την εκκίνηση, κατά τη διάρκεια της διαδικασίας και σε διάστημα 1 ημέρας και 30 ημερών μετά την επέμβαση. Τα αποτελέσματα συνοψίζονται στον **Πίνακα 1.5** και υποδεικνύουν ότι το FemoSeal™ VCS είναι ασφαλές και αποτελεσματικό για χρήση σε αυτόν τον πληθυσμό ασθενών.

**Πίνακας 1.5 Κλινικά αποτελέσματα που αναφέρθηκαν στη μελέτη πριν από την κυκλοφορία του προϊόντος στην αγορά**

|                                                                                                              | Μέρος 1    | Μέρος 2                 |
|--------------------------------------------------------------------------------------------------------------|------------|-------------------------|
| Αριθμός ασθενών                                                                                              | 20         | 60                      |
| Μέσος χρόνος επίτευξης αιμόστασης                                                                            | 1,2 λεπτά  | 1,6 λεπτά <sup>α</sup>  |
| Μέσος χρόνος έως το περιπατητικό στάδιο                                                                      | 72,2 λεπτά | 87,5 λεπτά <sup>β</sup> |
| Επιπολασμός σοβαρών αγγειακών επιπλοκών <sup>γ</sup>                                                         | 0 (0%)     | 1 (2%)                  |
| Αριθμός ασθενών με ανεπιθύμητα συμβάντα                                                                      | 5 (25%)    | 19 (32%)                |
| Αποτυχία θεραπείας (οριζόμενη ως σημαντικές αγγειακές επιπλοκές, ανάγκη μη αυτόματης συμπίεσης ή και τα δύο) | 0 (0%)     | 3 (5%)                  |
| Δυσλειτουργίες ιατροτεχνολογικού προϊόντος                                                                   | 0 (0%)     | 6 (10%)                 |

<sup>α</sup>Βάσει του συνολικού μεγέθους δείγματος 58, καθώς 2 ασθενείς δεν παρουσίασαν επίτευξη αιμόστασης κατά τη διάρκεια της διαδικασίας, λόγω προηγούμενων ομόπλευρων διατρήσεων. Αιμόσταση επιτεύχθηκε στα 7 λεπτά και στα 37 λεπτά σε αυτούς τους ασθενείς.

<sup>β</sup>Βάσει συνολικού μεγέθους δείγματος 59: 1 ασθενής δεν συμπεριλήφθηκε, καθώς τοποθετήθηκε σε αναπνευστήρα λόγω πνευμονικού οιδήματος και δεν ήταν περιπατητικός για περισσότερο από μία εβδομάδα.

<sup>γ</sup>Οριζόμενη ως αγγειακή επιπλοκή που απαιτεί μετάγγιση αίματος ή χειρουργική αποκατάσταση ή τοπική λοίμωξη που απαιτεί χορήγηση αντιβιοτικών, νοσηλεία ή παράταση της νοσηλείας ή χειρουργικό καθαρισμό του σημείου

Δεν παρατηρήθηκαν σοβαρές αγγειακές επιπλοκές στο Μέρος 1 της μελέτης. Αναφέρθηκε 1 σοβαρή αγγειακή επιπλοκή στο Μέρος 2 της μελέτης: ψευδοανεύρυσμα που αναφέρθηκε εντός μίας ημέρας μετά την επέμβαση. Για το συμβάν απαιτήθηκε συμπίεση με καθοδήγηση υπερηχογραφήματος και χορήγηση θρομβίνης στο ψευδοανεύρυσμα, ενώ παρατάθηκε η νοσηλεία του ασθενούς.

Από τα 5 ανεπιθύμητα συμβάντα που αναφέρθηκαν στο Μέρος 1 της μελέτης, παρουσιάστηκε 1 πιθανώς σχετιζόμενο με το ιατροτεχνολογικό προϊόν ανεπιθύμητο συμβάν: ένα μη σοβαρό συμβάν έντονης αιμορραγίας την 1η ημέρα μετεγχειρητικά. Από τα 19 ανεπιθύμητα συμβάντα

που αναφέρθηκαν στο Μέρος 2 της μελέτης, παρατηρήθηκαν 3 μη σοβαρά ανεπιθύμητα συμβάντα αιματώματος που σχετίζονται με το ιατροτεχνολογικό προϊόν και 6 πιθανώς σχετιζόμενα με το ιατροτεχνολογικό προϊόν μη σοβαρά συμβάντα, συμπεριλαμβανομένων 3 αναφορών εμμένοντος εξιδρώματος, 2 αιματωμάτων και 1 πόνου στα πόδια μετά την άσκηση.

Στο Μέρος 2 υπήρξαν 3 ασθενείς για τους οποίους η θεραπεία θεωρήθηκε αποτυχημένη: 2 λόγω αποτυχίας επίτευξης αιμόστασης χωρίς τη χρήση συμπίεσης και 1 λόγω της σοβαρής αγγειακής επιπλοκής (ψευδοανεύρυσμα). Δεν παρατηρήθηκαν αποτυχίες θεραπείας στο Μέρος 1 της μελέτης.

Από τις έξι δυσλειτουργίες του ιατροτεχνολογικού προϊόντος στο Μέρος 2 της μελέτης, τρεις δεν επηρέασαν τη διαδικασία, μία καταλογίστηκε σε σφάλμα του χρήστη, μία αφορούσε διαρροή του εισαγωγέα και μία θραύση άρθρωσης νήματος. Τα δύο τελευταία ζητήματα διευθετήθηκαν με ενημερώσεις μοντέλων που εφαρμόστηκαν το C11202.

Το Μέρος 2 της κλινικής μελέτης πριν από τη διάθεση στην αγορά δεν ανέφερε τα αποτελέσματα παρακολούθησης διάρκειας 6 μηνών, λόγω μη συμμόρφωσης του ασθενούς. Η κλινική μελέτη πριν από τη διάθεση στην αγορά (EU-SE-001) 30 ημερών, η οποία είναι σύμφωνη με τη χρονική περίοδο παρακολούθησης της κλινικής βιβλιογραφίας, καταδεικνύει ότι το FemoSeal™ VCS είναι ασφαλές και αποτελεσματικό.

#### 1.4.2 Σύνοψη δεδομένων από κλινικές έρευνες μετά από την κυκλοφορία του προϊόντος στην αγορά

Υπάρχουν 4 ολοκληρωμένες κλινικές μελέτες μετά την κυκλοφορία του προϊόντος στην αγορά που περιγράφονται στον Πίνακα 1.6 παρακάτω. Αυτές οι κλινικές έρευνες δεν δημοσιεύονται ή δεν είναι διαθέσιμες ηλεκτρονικά.

**Πίνακας 1.6 Κλινικές μελέτες μετά την κυκλοφορία του προϊόντος στην αγορά**

| Ολοκληρωμένες κλινικές μελέτες μετά την κυκλοφορία του προϊόντος στην αγορά                 |              |                                                                                                |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                 |                                                                                                                       |
|---------------------------------------------------------------------------------------------|--------------|------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|
| Όνομα μελέτης                                                                               | Έτος / CI    | Τύπος μελέτης                                                                                  | Στόχοι                                                                                                                                                                                                                                                                            | Ορόσημα                                                                                                                                                                         | Πιθανά κριτήρια αποδοχής                                                                                              |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI | Μελέτη μετά τη διάθεση στην αγορά, ενημέρωση μοντέλου του αποδοχή νέας συσκευασίας από χρήστες | Μελέτη μετά τη διάθεση στην αγορά, που πραγματοποιήθηκε στην ενημέρωση μοντέλου του Συστήματος σύγκλεισης FemoSeal Vascular® αριθ. 11202, το οποίο έχει ένα τροποποιημένο σύστημα χορήγησης σε σύγκριση με το πρώτο μοντέλο αριθ. 11200, για την τεκμηρίωση της λειτουργικότητας. | 100 ασθενείς<br>• 63 άνδρες / 37 γυναίκες<br>• Μέση ηλικία 68 ετών για γυναίκες, 65 ετών για άνδρες<br><br>2 συνηδικά νοσοκομεία, 6 ιατροί<br><br>112 ιατροτεχνολογικά προϊόντα | Αποτελέσματα<br>1. Εικόνες/ Οδηγίες στις ΟΧ που θεωρούνται κατατοπιστικές και επαρκείς<br>2. Άμεση αιμόσταση (91/100) |

|                                                                                   |                                                           |                                                     |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|-----------------------------------------------------------------------------------|-----------------------------------------------------------|-----------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|----|-----|----------|-------|----------|-----------|----|-----------|-----------|-------------------------|----------|--------------------|------------|---------------------|-----------|-------------------|---------|-----------------------|----------|--------------------------------|----------|----------------------|-----------|--------------------------|-----------|-----------------------------------|----------|----------------------|--------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                   |                                                           |                                                     | Στόχος της μελέτης ήταν η λήψη ανατροφοδότησης σχετικά με τις αναθεωρημένες Οδηγίες χρήσης (OX), το εκπαιδευτικό έργο για ιατρούς και νοσηλευτές, η επιβεβαίωση των αξιολογήσεων που πραγματοποιήθηκαν στην ανάλυση κινδύνων και η παροχή δεδομένων για τυχόν βελτιώσεις ποιότητας των προϊόντων. | Δεδομένα που καταγράφηκαν στα έντυπα αρχείων ασθενών (CRF)<br><br>Προγραμματισμένος χρόνος παρατήρησης – 30 λεπτά από τον χρόνο εφαρμογής                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008) | Dr. Nicolas Moes, Ιατρικό Πανεπιστήμιο Innsbruck, Αυστρία | Επιβεβαιωτική αξιολόγηση μετά τη διάθεση στην αγορά | Στόχος αυτής της μελέτης ήταν η αξιολόγηση της ασφάλειας και της απόδοσης του FemoSeal® κατά τη χρήση στο πλαίσιο της συνήθους κλινικής ρουτίνας σε ασθενείς που υποβάλλονται σε διαγνωστικό καρδιακό καθετηριασμό ή διαδερμική καρδιακή επέμβαση που πραγματοποιείται με θηκάρι 7F.              | 50 διαδοχικοί ασθενείς<br><br>Ενδειξη – διαγνωστικός ή επεμβατικός καρδιακός καθετηριασμός από την κοινή μηριαία αρτηρία<br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Πρωτεύοντα τελικά σημεία <ul style="list-style-type: none"><li>Πρωτεύον τελικό σημείο αποτελεσματικότητας – ΤΤΗ (χρόνος επίτευξης αιμόστασης) με ή χωρίς εξίδρωμα, αλλά χωρίς πρόσθετη συμπίεση, χειροκίνητη ή μηχανική.</li><li>Τελικό σημείο ασφάλειας – επιπολασμός ανεπιθύμητων συμβάντων – ελάσσονος σημασίας και σοβαρές αγγειακές επιπλοκές και όλα τα άλλα ανεπιθύμητα συμβάντα – σοβαρά και μη σοβαρά κατά τη διάρκεια της μελέτης (δηλ. μέχρι την έκδοση εξιτηρίου στον ασθενή).</li></ul> Αποτελέσματα <ul style="list-style-type: none"><li>Μέσος χρόνος επίτευξης αιμόστασης</li><li>Διαγνωστική - 56,6 ± 29 δευτερόλεπτα</li><li>Επεμβατική 59,9 ± 16,2 δευτερόλεπτα</li><li>Όλοι οι ασθενείς 57,8 ± 26,3</li><li>Όλοι οι ασθενείς είχαν δυνατότητα να καταστούν περιπατητικοί μετά από 4 ώρες ανάπαυσης χωρίς προβλήματα.</li></ul> Αποτελέσματα ασφάλειας <ul style="list-style-type: none"><li>49/50 (98%) χωρίς αγγειακές επιπλοκές μέχρι την έκδοση εξιτηρίου από το νοσοκομείο</li></ul> |
| n                                                                                 | 50                                                        |                                                     |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| men                                                                               | 35 (70%)                                                  |                                                     |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| women                                                                             | 15 (30%)                                                  |                                                     |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| PCI cases                                                                         | 15                                                        |                                                     |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| age (yrs)                                                                         | 62.8±11.1                                                 |                                                     |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| body mass index (kg/m²)                                                           | 25.4±6.7                                                  |                                                     |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| systolic BP (mmHg)                                                                | 131.2±20.9                                                |                                                     |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| diastolic BP (mmHg)                                                               | 77.9±10.6                                                 |                                                     |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| diabetes mellitus                                                                 | 9 (18%)                                                   |                                                     |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| arterial hypertension                                                             | 34 (68%)                                                  |                                                     |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| previous coronary intervention                                                    | 13 (26%)                                                  |                                                     |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| preprocedure aspirin                                                              | 50 (100%)                                                 |                                                     |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| preprocedure clopidogrel                                                          | 50 (100%)                                                 |                                                     |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Procedural unfractionated heparin                                                 | 15 (30%)                                                  |                                                     |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Procedural abciximab                                                              | 2 (4%)                                                    |                                                     |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |

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|                                                                                                                                 |                                 |                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | <ul style="list-style-type: none"> <li>Μέσος χρόνος έκδοσης εξιτηρίου 2,6 ημέρες</li> <li>1/50 (2%) μικρή αιμορραγία την επόμενη ημέρα μετά από κινητοποίηση χωρίς προβλήματα την ημέρα της αγγειογραφίας</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | 2009 RADI                       | Μελέτη μετά τη διάθεση στην αγορά                                               | <p>Η μελέτη θα πρέπει να αναφέρει εάν οι πελάτες/χρήστες αντιλήφθηκαν τυχόν προβλήματα με τη νέα συσκευασία, ειδικά τη μη αποστειρωμένη εξωτερική πλευρά της σακούλας Tuvek/PET-PE.</p> <p>Η μελέτη θα πρέπει επίσης να παρέχει πληροφορίες σχετικά με το εάν ο θεράπων ιατρός αντιλαμβάνεται τυχόν διαφορές στα βήματα εφαρμογής/ έκπτυξης του προϊόντος σε σύγκριση με τα προηγούμενα ιατροτεχνολογικά προϊόντα.</p> <p>Η μελέτη θα πρέπει επίσης να παρέχει στοιχεία για τυχόν περαιτέρω ανάγκες βελτίωσης της ποιότητας του προϊόντος.</p> | <p>25 ιατροτεχνολογικά προϊόντα</p> <p>4 σουηδικά νοσοκομεία</p> <p>16/25 (64%) των ασθενών ήταν ασθενείς με διαδερμική στεφανιαία παρέμβαση (PCI) που λάμβαναν ισχυρά αντιπηκτικά φάρμακα</p>                                                                                                                                                                                                                                                                             | <p>Αποτελέσματα</p> <ol style="list-style-type: none"> <li>1. Προβλήματα που σχετίζονται με τη συσκευασία – 21/25 (84%) εφαρμογές ήταν επιτυχείς. 4/25 (16%) ήταν ανεπιτυχείς (1 - δοκιμή νέου εισαγωγέα, 1 εσωτερικός δίσκος πέρασε μέσω της αρτηριοτομής στο βήμα στήριξης, το κουμπί ανέβηκε και ο εξωτερικός δίσκος τοποθετήθηκε στον πόρο του ιστού τομής, 2 δεν επιτεύχθηκε άμεση αιμόσταση παρότι δεν παρατηρήθηκαν ζητήματα έκπτυξης.)</li> <li>2. Άμεση αιμόσταση 19/25 (76%) ασθενείς</li> <li>3. Αιμορραγία 11/25 (44%) – 9/25 (36%) εξίδρωμα/ αιμορραγία, 2/25 (8%) αιματώματα</li> </ol> <p>Συνολικό ποσοστό συμβάντων 19%</p> |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022) | 2022/Terumo Medical Corporation | Προοπτική, πολυκεντρική παρατήρηση μετά την κυκλοφορία του προϊόντος στην αγορά | <p>Στόχος είναι η περαιτέρω κατάδειξη της ασφάλειας και της αποτελεσματικότητας του FemoSeal™ VCS στην επίτευξη αιμόστασης στο σημείο προσπέλασης της κοινής μηριαίας αρτηρίας (ΚΜΑ) σε πραγματικούς ασθενείς που υποβάλλονται σε διαδερμικές ενδοαγγειακές επεμβάσεις</p>                                                                                                                                                                                                                                                                     | <ul style="list-style-type: none"> <li>• Παρακολούθηση ασθενών σε 30 ημέρες (<math>\pm</math> 7 ημέρες) με επίσκεψη στο νοσοκομείο ή τηλεφωνική κλήση.</li> <li>• Ένταξη: Δεκέμβριος 2021 έως Ιούλιος 2022.</li> <li>• 230 ενταγμένα άτομα που υποβάλλονται σε διαγνωστικές ή επεμβατικές ενδοαγγειακές διαδικασίες στις οποίες χρησιμοποιείται το FemoSeal™.</li> </ul> <p>3 κέντρα στην Ευρώπη: Γαλλία (92 ασθενείς), Γερμανία (38 ασθενείς), Βέλγιο (100 ασθενείς).</p> | <ul style="list-style-type: none"> <li>• <b>Δημογραφικά στοιχεία/ συννοσηρότητες:</b> <ul style="list-style-type: none"> <li>- Φύλο: 161 άνδρες (70%)/ 69 γυναίκες 69 (30%).</li> <li>- Μέση ηλικία: 70 <math>\pm</math> 12.</li> <li>- ΔΜΣ: 26,1 <math>\pm</math> 4,95 kg/m2.</li> <li>- Υπέρταση: 160 ασθενείς (69,6%).</li> <li>- Δυσλιπιδαιμία: 128 (55,7%).</li> <li>- Στεφανιαία νόσος: 42 (18,3%).</li> <li>- Σημερινός καπνιστής: 86 (37,6 %).</li> <li>- Πρώην καπνιστής: 66 (28,8%).</li> </ul> </li> </ul>                                                                                                                       |

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|  |  |  |  |  | <ul style="list-style-type: none"> <li>- Στεφανιαία νόσος: 34 (14%).</li> <li>- Προηγούμενο οξύ έμφραγμα του μυοκαρδίου: 18 (7,8 %).</li> <li>- Επαναγγείωση περιφερικής αρτηρίας: 12 (5,2%) καρωτιδική και 83 (37,5%) και αρτηρία κάτω άκρου.</li> <li>- Αντιαρροπιακή θεραπεία (κατά την έναρξη της μελέτης): 211 (91,7%), συμπεριλαμβανομένης της διπλής αντιαρροπιακής θεραπείας (DAPT) 21 (9,1%).</li> <li>- Από του στόματος αντιπηκτική αγωγή: 40 (17,4%) ασθενείς.</li> </ul> <p>• <b>Χαρακτηριστικά παρέμβασης:</b></p> <ul style="list-style-type: none"> <li>- Περιβάλλον: 162 εσωτερικά περιστατικά (70,4%), 68 εξωτερικά περιστατικά (29,6%).</li> <li>- Κύρια ένδειξη: χολόλιθος 147 περιστατικά (63,9%).</li> <li>- Προσπέλαση: 35 ορθόδρομη (15,3%), 194 αντίδρομη (84,7%).</li> </ul> <p>• <b>Πρωτεύοντα τελικά σημεία:</b></p> <ul style="list-style-type: none"> <li>- Συνδυασμένη ασφάλεια (απουσία σημαντικών επιπλοκών του άκρου του σημείου προσπέλασης εντός 6 ωρών μετεγχειρητικά) και επίτευξη αποτελεσματικότητας (επιτυχής αιμόσταση στο σημείο παρακέντησης) τελικού σημείου σε 215/226 (95,1%) [95% CI: 91,46, 97,55] ασθενείς στην ομάδα πλήρους ανάλυσης (FAS) και 215/230 (93,5%)</li> </ul> |
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|  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
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|  |  |  |  |  | <p>[95% CI 89,47, 96,30] στην ομάδα χρήσης του FemoSeal™.</p> <p>- Το τελικό σημείο αποτελεσματικότητας επιτεύχθηκε σε 219/226 (96,9%) CI [93,7, 98,7] ασθενείς.</p> <p>- Το τελικό σημείο ασφάλειας επιτεύχθηκε σε 220/230 (95,2%) [95% CI: 92,15, 97,90] ασθενείς.</p> <p>• <b>Δευτερεύοντα τελικά σημεία:</b></p> <p>- Απουσία επιπλοκών ελάσσονος σημασίας στο σημείο προσπέλασης για έξι ώρες μετεγχειρητικά επιτεύχθηκε σε 225/230 ασθενείς (97,8%) [95% CI: 95,00, 99,29].</p> <p>- Απουσία επιπλοκών μείζονος και ελάσσονος σημασίας στο σημείο προσπέλασης από έξι ώρες έως 30 ημέρες μετεγχειρητικά επιτεύχθηκε σε 219/230 (95,2%) [95% CI:91,60, 97,59] ασθενείς.</p> <p>- Διάμεσος χρόνος επίτευξης αιμόστασης με το FemoSeal™ VCD: 0,42 (0,25, 0,50) λεπτά.</p> <p>- Διάμεσος χρόνος έως το περιπατητικό στάδιο: 5,00 (4,54, 5,50) λεπτά.</p> <p>- Διάμεση διάρκεια παραμονής στο νοσοκομείο: 23,98 (22,72, 25,00) ώρες.</p> <p>- Χρησιμότητα του FemoSeal™ VCS: «εύκολη» ή «πολύ εύκολη» έκπτυξη σε 98,7% των περιστατικών («εύκολη» έκπτυξη σε 21 (9,2%), «πολύ εύκολη» έκπτυξη σε 205 (89,5%)) με μηδενική ή χαμηλή</p> |
|--|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|



|  |  |  |  |  |                                                                                                                                                                                                                                                                                       |
|--|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | αντίσταση στην έκπτυξη σε 226 (98,3%) των περιστατικών.<br>Σε 152/230 (66,1%) ασθενείς χρησιμοποιήθηκε οδηγό σύρμα που περιλαμβάνεται στο κιτ FemoSeal™ (GW 0,038") και συνιστάται στο FemoSeal™ χωρίς αναφερόμενες ελλείψεις του ιατροτεχνολογικού προϊόντος ή ανεπιθύμητα συμβάντα. |
|--|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Η μελέτη του 2006 πραγματοποιήθηκε για την επιβεβαίωση της ασφάλειας και της αποτελεσματικότητας του τρέχοντος ιατροτεχνολογικού προϊόντος με ένα βελτιωμένο σύστημα χορήγησης και για τη λήψη ανατροφοδότησης σχετικά με τις οδηγίες χρήσης και το πρόγραμμα εκπαίδευσης του FemoSeal™ VCS. Η μελέτη περιελάμβανε 100 ασθενείς και το πρωτεύον τελικό σημείο ήταν η επίτευξη αιμόστασης ή η ανάγκη πρόσθετων χειροκίνητων ή μηχανικών συμπίεσεων. Αυτή η μελέτη κατέληξε στο συμπέρασμα ότι η εφαρμογή του FemoSeal™ VCS ήταν επιτυχής στην πλειοψηφία των περιπτώσεων (91% επίτευξη άμεσης αιμόστασης).

Η μελέτη του 2008 περιελάμβανε 50 ασθενείς για την αξιολόγηση της ασφάλειας και της απόδοσης του FemoSeal™ VCS κατά την χρήση στη συνήθη κλινική ρουτίνα σε ασθενείς που υποβάλλονται σε καρδιακό καθετηριασμό με θηκάρι 7 Fr. Το πρωτεύον τελικό σημείο για τη μελέτη ήταν η συλλογή δεδομένων σχετικά με τον χρόνο επίτευξης αιμόστασης και τον χρόνο έως το περιπατητικό στάδιο χωρίς πρόσθετη συμπίεση, χειροκίνητη ή μηχανική. Τα αποτελέσματα της μελέτης κατέληξαν στο συμπέρασμα ότι ο μέσος χρόνος επίτευξης αιμόστασης ήταν 57,8 δευτερόλεπτα και όλοι οι ασθενείς ήταν δυνατό να μεταβούν στο περιπατητικό στάδιο μετά από 4 ώρες ανάπαυσης.

Η μελέτη του 2009 αφορούσε την αξιολόγηση της νέας συσκευασίας του FemoSeal™ VCS. Στη μελέτη συμπεριλήφθηκαν 25 ασθενείς. Το πρωτεύον τελικό σημείο αφορούσε το εάν ο χρήστης αντιμετώπισε προβλήματα με τη συσκευασία. Οι χρήστες δεν εντόπισαν προβλήματα σχετικά με τη νέα συσκευασία του FemoSeal™ VCS. Από αυτήν τη μελέτη συγκεντρώθηκαν επίσης δεδομένα για τον χρόνο επίτευξης αιμόστασης.

Η μελέτη του 2022 αποσκοπούσε στην προληπτική συλλογή δεδομένων ασφάλειας και αποτελεσματικότητας του FemoSeal VCS στην επίτευξη αιμόστασης στο σημείο προσπέλασης της κοινής μηριαίας αρτηρίας (ΚΜΑ) σε πραγματικούς ασθενείς που υποβάλλονται σε διαδερμικές ενδοαγγειακές επεμβάσεις. Στη μελέτη συμπεριλήφθηκαν 230 ασθενείς. Τα πρωτεύοντα τελικά σημεία για το μητρώο είναι η επιτυχία της επέμβασης (δηλ. επιτυχής αιμόσταση στο σημείο διάτρησης) και η μείωση σοβαρών επιπλοκών (π.χ. αγγειακός τραυματισμός, αιμορραγία που σχετίζεται με το σημείο προσπέλασης, μόλυνση στο σημείο

προσπέλασης, επαναλαμβανόμενη χειροκίνητη συμπίεση και ομόπλευρη οξεία ισχαιμία άκρου που σχετίζεται με το νέο σημείο προσπέλασης). Η μελέτη κατέληξε στο συμπέρασμα ότι το FemoSeal™ VCS αποδίδει καλά σε πραγματικές συνθήκες και παρέχει αποτελεσματική αιμόσταση και χαμηλά ποσοστά επιπλοκών στο σημείο προσπέλασης για ασθενείς που υποβάλλονται σε περιφερικές ενδοαγγειακές επεμβάσεις. Καταδεικνύει καλές επιδόσεις με σύντομο χρόνο επίτευξης αιμόστασης και καλή ανατροφοδότηση σχετικά με τη χρηστικότητα από τον χειριστή, γεγονός που καθιστά το FemoSeal™ VCS ένα πολύτιμο ιατροτεχνολογικό προϊόν για τη σύγκλειση μηριαίας προσπέλασης.

### 1.4.3 Σύνοψη δεδομένων από την κλινική παρακολούθηση μετά από την κυκλοφορία του προϊόντος στην αγορά

#### 1.4.3.1 Ολοκληρωμένες δραστηριότητες κλινικής παρακολούθησης μετά την κυκλοφορία του προϊόντος στην αγορά

Μια περίληψη των ολοκληρωμένων δραστηριοτήτων κλινικής παρακολούθησης μετά την κυκλοφορία στην αγορά περιγράφεται στον **Πίνακα 1.7** παρακάτω.

**Πίνακας 1.7. Δραστηριότητες κλινικής παρακολούθησης μετά την κυκλοφορία του προϊόντος στην αγορά**

| Ολοκληρωμένες δραστηριότητες κλινικής παρακολούθησης μετά την κυκλοφορία του προϊόντος στην αγορά |          |                                                                                       |                                                                                                                                                                                     |                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|---------------------------------------------------------------------------------------------------|----------|---------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Ονομασία δραστηριότητας                                                                           | Έτος/ CI | Τύπος μελέτης                                                                         | Στόχοι                                                                                                                                                                              | Ορόσημα                                                                                                                                                 | Πιθανά κριτήρια αποδοχής                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021)                         | 2021 TMC | Κλινική έρευνα μετά την κυκλοφορία του προϊόντος στην αγορά - έρευνα υψηλής ποιότητας | Έρευνα μετά την κυκλοφορία στην αγορά για τη συλλογή προοπτικών σχολίων σχετικά με τη χρήση του FemoSeal™ Vascular Closure Device που διανέμεται στις αγορές της Ευρωπαϊκής Ένωσης. | <ul style="list-style-type: none"> <li>120 περιπτώσεις</li> <li>8 μοναδικοί ιατροί με &gt; 5 έτη εμπειρίας</li> <li>Πολλές χώρες στην Ευρώπη</li> </ul> | <p><b>Αξιολογήσεις ιατροτεχνολογικών προϊόντων σε κλίμακα 1-5 - Δηλώσεις έρευνας</b></p> <ul style="list-style-type: none"> <li>Κριτήρια αποδοχής <ul style="list-style-type: none"> <li>Οι αξιολογήσεις 3-5 θεωρούνται ευνοϊκές</li> <li>Όλες οι δηλώσεις πρέπει να έχουν ≥ 80% θετική ανατροφοδότηση</li> </ul> </li> <li>Αποτελέσματα <ul style="list-style-type: none"> <li>Καμία δήλωση έρευνας δεν έλαβε &gt; 20% μη ευνοϊκές απαντήσεις</li> </ul> </li> </ul> |

| Ολοκληρωμένες δραστηριότητες κλινικής παρακολούθησης μετά την κυκλοφορία του προϊόντος στην αγορά                               |                  |                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|---------------------------------------------------------------------------------------------------------------------------------|------------------|---------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                 |                  |                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                  | <ul style="list-style-type: none"> <li>Δεν έχουν υποβληθεί καταγγελίες για το προϊόν</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                             |
| 20210298 – 0.035” and 0038” Guidewire Clinical Survey Report (2021)                                                             | 2021 TMC         | Κλινική έρευνα μετά την κυκλοφορία του προϊόντος στην αγορά - έρευνα υψηλής ποιότητας | Έρευνα μετά την κυκλοφορία του προϊόντος στην αγορά για τη συλλογή προοπτικών σχολίων σχετικά με τη χρήση του οδηγού σύρματος 0,035” που συμπεριλαμβάνεται στο 6Fr Angio-Seal™ VIP Vascular Closure Device (VCD) και του οδηγού σύρματος 0,038” που συμπεριλαμβάνεται τόσο στο 8Fr Angio-Seal™ VIP VCD όσο και στο FemoSeal Vascular Closure System που διανέμεται στις αγορές της Ευρωπαϊκής Ένωσης. | <ul style="list-style-type: none"> <li>Έρευνες για σύρμα 0,035” <ul style="list-style-type: none"> <li>106 έρευνες</li> <li>64 ιατροί</li> </ul> </li> <li>Έρευνες για σύρμα 0,038” <ul style="list-style-type: none"> <li>109 έρευνες</li> <li>55 ιατροί</li> </ul> </li> <li>12 αναδρομικές έρευνες</li> </ul> | <b>Αξιολογήσεις ιατροτεχνολογικών προϊόντων σε κλίμακα 1-5 - Δηλώσεις έρευνας</b> <ul style="list-style-type: none"> <li>Κριτήρια αποδοχής <ul style="list-style-type: none"> <li>Οι αξιολογήσεις 3-5 θεωρούνται ευνοϊκές</li> <li>Όλες οι δηλώσεις πρέπει να έχουν <math>\geq 80\%</math> θετική ανατροφοδότηση</li> </ul> </li> <li>Αποτελέσματα <ul style="list-style-type: none"> <li>Όλα τα οδηγία σύρματα έλαβαν αποδεκτές αξιολογήσεις</li> <li>Δεν έχουν υποβληθεί καταγγελίες για το προϊόν</li> </ul> </li> </ul> |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024 TMC/TE | Κλινική έρευνα μετά την κυκλοφορία του προϊόντος στην αγορά - έρευνα υψηλής ποιότητας | Για την προοπτική συλλογή σχολίων σχετικά με τη χρήση του FemoSeal VCS με οδηγία σύρματα που διανέμονται στην αγορά της ΕΕ.                                                                                                                                                                                                                                                                           | <ul style="list-style-type: none"> <li>126 έρευνες</li> <li>7 κέντρα</li> <li>5 χώρες</li> <li>14 Νοεμβρίου 2023 - 11 Ιουνίου 2024</li> <li>Ιατρική ειδικότητα: <ul style="list-style-type: none"> <li>Αγγειοχειρουργική</li> <li>Επεμβατική ακτινολογία</li> <li>Αγγειολογία</li> </ul> </li> </ul>             | <b>Αξιολογήσεις ιατροτεχνολογικών προϊόντων σε κλίμακα 5 - Δηλώσεις έρευνας</b> <ul style="list-style-type: none"> <li>Κριτήρια αποδοχής <ul style="list-style-type: none"> <li>Οι αξιολογήσεις 3-5 θεωρούνται ευνοϊκές</li> <li>Όλες οι δηλώσεις πρέπει να έχουν <math>\geq 80\%</math> θετική ανατροφοδότηση</li> <li>Εάν προκύψουν ανεπιθύμητα συμβάντα σε</li> </ul> </li> </ul>                                                                                                                                        |

| Ολοκληρωμένες δραστηριότητες κλινικής παρακολούθησης μετά την κυκλοφορία του προϊόντος στην αγορά |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|---------------------------------------------------------------------------------------------------|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                   |  |  |  |  | <div>           αυτήν την έρευνα, θα πρέπει να είναι αυτά που αναμένονται από τη διαχείριση κινδύνου.         </div> <div> <ul style="list-style-type: none"> <li>               Δημογραφικά στοιχεία ασθενών               <ul style="list-style-type: none"> <li>                   Γυναίκες: 29,4% (37/126)                 </li> <li>                   Άνδρες: 69,8% (88/126)                 </li> <li>                   Μη αναφερόμενο φύλο: 0,8 (1/126)                 </li> <li>                   Ηλικία &gt;75 ετών: 31,7%                 </li> </ul> </li> <li>               Αποτελέσματα               <ul style="list-style-type: none"> <li>                   Το οδηγό σύρμα που παρέχεται με το FemoSeal™ VCS: 101/126 (80,2%).                 </li> <li>                   Διάρκεια διαδικασίας (λεπτά): 63,4 (36,6) (μέση τιμή (SD)), 57,0 (36,0-81,0) (διάμεση τιμή (IQR))                 </li> <li>                   Όλες οι αξιολογήσεις απόδοσης του FemoSeal™ VCS ήταν ευνοϊκές.                 </li> <li>                   Όλες οι αξιολογήσεις του οδηγού σύρματος που παρέχεται από                 </li> </ul> </li> </ul> </div> |

| Ολοκληρωμένες δραστηριότητες κλινικής παρακολούθησης μετά την κυκλοφορία του προϊόντος στην αγορά |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                |
|---------------------------------------------------------------------------------------------------|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                   |  |  |  |  | <div> <div>το FemoSeal™ VCS ήταν ευνοϊκές.</div> <div> <div>ο Ένα (0,8%) ανεπιθύμητο συμβάν: οι δίσκοι FemoSeal™ VCS δεν ευθυγραμμίστηκαν καλά πιθανώς λόγω της χρήσης άκαμπτου οδηγού σύρματος (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 ίντσες) που απαιτεί χειροκίνητη συμπίεση για την επίτευξη αιμόστασης.</div> </div> </div> |

Η Terumo Medical Corporation ολοκλήρωσε τρεις έρευνες υψηλής ποιότητας για ιατρικούς χρήστες κατά την τρέχουσα περίοδο αναφοράς (01 Σεπτεμβρίου 2019 - 31 Αυγούστου 2024).

Από τις κλινικές έρευνες για το FemoSeal™ συλλέχθηκαν προληπτικά κλινικά δεδομένα σε σχέση με την ασφάλεια και την απόδοση του FemoSeal™ VCS κατά τη διάρκεια της κλινικής χρήσης. Η έρευνα περιλάμβανε ερωτήσεις που εστίαζαν στο ιατροτεχνολογικό προϊόν συνολικά και στα σχετικά παρελκόμενα, συμπεριλαμβανομένου του οδηγού σύρματος 0,038", καθώς και στις άμεσες αλληλεπιδράσεις τους. Από τις κλινικές έρευνες για το οδηγό σύρμα συλλέχθηκαν προληπτικά κλινικά δεδομένα σε σχέση με την ασφάλεια και τις επιδόσεις κατά τη διάρκεια της κλινικής χρήσης του οδηγού σύρματος 0,038" που παρέχεται με το FemoSeal™ VCS. Οι ερωτήσεις της έρευνας επικεντρώθηκαν ειδικά στη γενική χρήση του οδηγού σύρματος, από την εισαγωγή του μέσω του επεμβατικού θηκαριού στο αγγειακό σύστημα έως και την αφαίρεσή του.

Το FemoSeal™ VCS και το οδηγό σύρμα 0,038" που περιλαμβάνεται στο ιατροτεχνολογικό προϊόν έλαβαν όλες τις αποδεκτές αξιολογήσεις και υποβλήθηκαν έξι (6) καταγγελίες για το ιατροτεχνολογικό προϊόν και εννέα (9) μη καταγγελίες για το οδηγό σύρμα με βάση την αξιολόγηση των σχολίων που ελήφθησαν από υψηλής ποιότητας κλινικές έρευνες. Οι καταγγελίες αξιολογήθηκαν τόσο για το FemoSeal όσο και για το οδηγό σύρμα και αξιολογήθηκαν ως μέρος της διαδικασίας παρακολούθησης μετά τη διάθεση στην αγορά της Terumo. Δεν εντοπίστηκαν νέοι κίνδυνοι ή/και επίπεδα κινδύνου.

Μια έρευνα σε ιατρούς χρήστες ολοκληρώθηκε το 2024 στο πλαίσιο δραστηριοτήτων PMCF. Τα αποτελέσματα της έρευνας κατέδειξαν ότι η βαθμολογία απόδοσης και η ασφάλεια του FemoSeal™ VCS ήταν συνολικά πολύ ευνοϊκές. Έχει επίσης καταδειχθεί η συμβατότητα άλλων οδηγών συρμάτων εκτός από το ένα πρότυπο που παρέχεται με το FemoSeal™ VCS.

#### **1.4.3.2 Συνεχής/ προγραμματισμένη κλινική παρακολούθηση μετά την κυκλοφορία του προϊόντος στην αγορά**

Η TMC πραγματοποιεί μία συνεχιζόμενη/ προγραμματισμένη κλινική δραστηριότητα παρακολούθησης μετά τη διάθεση στην αγορά. Θα πραγματοποιηθεί μια κλινική έρευνα για την προληπτική συλλογή σχολίων και παρατηρήσεων σε σχέση με τη χρήση του οδηγού σύρματος που συνοδεύει το FemoSeal VCS και διατίθεται στην ευρωπαϊκή αγορά. Η έρευνα θα ολοκληρωθεί από ιατρούς για να μελετηθεί ποια οδηγά σύρματα χρησιμοποιήθηκαν κατά την επέμβαση. Σκοπός αυτής της έρευνας είναι η αντιμετώπιση ενός κενού που εντοπίστηκε ως έλλειψη βιβλιογραφίας και σχολίων εξωτερικών αναθεωρητών σχετικά με τη συμβατότητα του FemoSeal™ VCS με τη χρήση άλλων οδηγών συρμάτων άλλων κατασκευαστών εκτός της Terumo. Στα σχόλια και τις παρατηρήσεις συμπεριλαμβάνονται τεχνικά αποτελέσματα, καθώς και η κλινική απόδοση και η ασφάλεια που αφορούν στην απόδοση του ιατροτεχνολογικού προϊόντος με διαφορετικά οδηγά σύρματα.

#### **1.4.4 Σύνοψη δεδομένων από συστηματική ανασκόπηση της βιβλιογραφίας**

Η Terumo Medical Corporation διενεργεί συστηματικά ανασκόπηση της βιβλιογραφίας, προκειμένου να συλλέξει και να αξιολογήσει δεδομένα κλινικής ασφάλειας και απόδοσης από δημοσιευμένες μελέτες για το FemoSeal™ VCS ή/και παρόμοια ιατροτεχνολογικά προϊόντα. Ο σκοπός του ετήσιου ελέγχου της δημοσιευμένης βιβλιογραφίας είναι ο εντοπισμός προηγούμενων άγνωστων ανεπιθύμητων ενεργειών, η παρακολούθηση γνωστών ανεπιθύμητων ενεργειών, ο εντοπισμός έκτακτων κινδύνων και ο εντοπισμός πιθανής συστηματικής κακής χρήσης ή χρήσης εκτός εγκεκριμένων ενδείξεων του FemoSeal™ VCS.

Κατά την πιο πρόσφατη συστηματική ανασκόπηση της βιβλιογραφίας, η οποία κάλυψε την περίοδο από την 1η Σεπτεμβρίου 2019 έως την 31η Αυγούστου 2024, εντοπίστηκαν 29 δημοσιευμένες μελέτες που παρείχαν δεδομένα κλινικής ασφάλειας και απόδοσης για το FemoSeal™ VCS. Είκοσι τρεις βιβλιογραφικές παραπομπές ανέφεραν χρήση του FemoSeal™

VCS εντός της επισήμανσης, ενώ χρήση εκτός επισήμανσης αναφέρθηκε σε εννέα μελέτες. Γενικά, από την ανασκόπηση της βιβλιογραφίας όσον αφορά σε μελέτες που εστιάζουν ειδικά στη χρήση του FemoSeal™ VCS προκύπτει ότι ο υπό μελέτη πληθυσμός είναι αντιπροσωπευτικός των ασθενών της ΕΕ που υποβάλλονται σε επεμβάσεις διαδερμικού αγγειακού καθετηριασμού. Βλ. **Ενότητα 3** για έναν κατάλογο αυτών των 23 δημοσιεύσεων εντός της επισήμανσης, με αξιολόγηση από ομοτίμους.

Οι κλινικές επιδόσεις αξιολογήθηκαν με βάση τις ακόλουθες μετρήσεις:

- Ο χρόνος επίτευξης αιμόστασης είναι καλύτερος ή συγκρίσιμος με τις τελευταίες εξελίξεις στην τεχνολογία για τη διαδερμική σύγκλειση της κοινής μηριαίας αρτηρίας.
- Ο χρόνος έως το περιπατητικό στάδιο είναι καλύτερος ή συγκρίσιμος με τις τελευταίες εξελίξεις στην τεχνολογία για τη διαδερμική σύγκλειση της κοινής μηριαίας αρτηρίας.
- Το ποσοστό των μετεγχειρητικών επιπλοκών είναι συγκρίσιμο ή χαμηλότερο από τα ισχύοντα πρότυπα περίθαλψης.

Με βάση αυτές τις μετρήσεις κλινικής απόδοσης, τα δεδομένα σε αυτήν την ανασκόπηση βιβλιογραφίας έδειξαν ότι το FemoSeal™ VCS μπορεί να χρησιμοποιηθεί με επιτυχία στη σύγκλειση της διάτρησης μηριαίας αρτηρίας (αρτηριοτομή) σε ασθενείς που έχουν υποβληθεί σε διαδερμικό καθετηριασμό με χρήση ενός επεμβατικού θηκαριού 7 Fr ή μικρότερου. Η πλήρης αιμόσταση επιτεύχθηκε στην πλειοψηφία των ασθενών (79,65-100%) και συσχετίστηκε με διάμεσο χρόνο έως την αιμόσταση το 0,5 λεπτό και μέσο χρόνο έως το εξιτήριο τις 3 ημέρες. Ποσοστό από 69,2 έως 86,7% των ασθενών κατέστησαν περιπατητικοί 5 ώρες μετά τη σύγκλειση, με μέσο παραμονή σε κλινήρη θέση μετεγχειρητικά τα 349 λεπτά. Η αστοχία του FemoSeal™ VCS παρατηρήθηκε σε ποσοστό 3,68-4% των περιστατικών και απαιτήθηκε πρόσθετη χειροκίνητη συμπίεση σε ποσοστό 0,9-4,4% των διαδικασιών.

Η κλινική ασφάλεια αξιολογήθηκε με βάση τα ανεπιθύμητα συμβάντα, συμπεριλαμβανομένων, μεταξύ άλλων, των εξής:

- Αιμορραγία
- Αιμάτωμα
- Ψευδοανεύρυσμα
- Μώλωπες
- Αρτηριοφλεβικό συρίγγιο
- Μόλυνση
- Θάνατος



Για καθένα από αυτά τα ανεπιθύμητα συμβάντα, το ποσοστό εμφάνισης που αναφέρθηκε για το FemoSeal™ VCS στις συμπεριλαμβανόμενες μελέτες ήταν μικρότερο ή συγκρίσιμο με τα ποσοστά που είχαν αναφερθεί στο παρελθόν για χειροκίνητη συμπίεση και άλλα ιατροτεχνολογικά προϊόντα σύγκλεισης αγγείων.

Η ανασκόπηση 10 αναφορών περιστατικών δεν κατέδειξε ανεπιθύμητα συμβάντα, καθώς δεν εντοπίστηκαν νέοι, μη αναμενόμενοι, αναδυόμενοι ή μη αποδεκτοί κίνδυνοι.

Η συνολική αποτελεσματικότητα της χρήσης του FemoSeal™ VCS κατά τη διάρκεια διαγνωστικής αγγειογραφίας ή παρεμβατικών επεμβάσεων εξαρτάται από πολλούς παράγοντες, όπως: φύλο, ηλικία, ανατομία ασθενούς, συννοσηρότητες, ανατομική τοποθέτηση του σημείου παρακέντησης, εμπειρία του χειρουργού, μέθοδος έκπτυξης του VCD, μετεγχειρητική φροντίδα κ.λπ. Εκτός από την τεχνική επιτυχία, συμπεριλαμβανομένης της επίτευξης αιμόστασης, το FemoSeal™ VCS προσέφερε κλινικά οφέλη σε σχέση με τη σύγκλειση αγγείων μετά από παρακέντηση της μηριαίας αρτηρίας, όπως μείωση του χρόνου έως την επίτευξη αιμόστασης, μείωση του χρόνου έως ότου οι ασθενείς καταστούν περιπατητικοί. Τα αποτελέσματα επιδόσεων για το FemoSeal™ VCS συνάδουν με τα αναμενόμενα για τον συγκεκριμένο τύπο ιατροτεχνολογικού προϊόντος όταν χρησιμοποιείται όπως προβλέπεται. Ορισμένες από τις αναφορές που ανακτήθηκαν κατά τη διάρκεια της τρέχουσας περιόδου αναζήτησης κατέδειξαν τη χρήση του εν λόγω τεχνολογικού προϊόντος σε ανατομική θέση διαφορετική από την κοινή μηριαία αρτηρία και για τη σύγκλειση αρτηριοτομών > 7 Fr, η οποία θεωρείται εκτός επισήμανσης.

Κατά την ανασκόπηση δεν εντοπίστηκαν άγνωστες ανεπιθύμητες ενέργειες, αναδυόμενοι κίνδυνοι ή πιθανή συστηματική εσφαλμένη χρήση του προϊόντος. Ωστόσο, εάν το FemoSeal™ VCS χρησιμοποιείται με προσοχή από εκπαιδευμένους ιατρούς, αποτελεί χρήσιμο και απαραίτητο ιατροτεχνολογικό προϊόν κλινικής χρήσης. Συνολικά, η στοχευόμενη θεραπεία και, κατά συνέπεια, το FemoSeal™ VCS ανταποκρίνεται στην κλινική ανάγκη που υπάρχει επί του παρόντος στη θεραπεία επιπλοκών που σχετίζονται με την αγγειακή προσπέλαση.

Συνολικά, από τα δεδομένα αυτής της βιβλιογραφικής ανασκόπησης δεν εντοπίστηκε κανένα ζήτημα απόδοσης ή ασφάλειας στο κλινικό περιβάλλον που ήταν άγνωστο στο παρελθόν ή ανεπιθύμητες επιπτώσεις που παρουσιάστηκαν σε υψηλότερα από τα αναμενόμενα/ αποδεκτά ποσοστά. Επομένως, μπορεί να συναφθεί από αυτήν την επισκόπηση βιβλιογραφίας ότι το FemoSeal™ VCS, όταν χρησιμοποιείται για την παροχή συμπίεσης για αιμόσταση στην αρτηριοτομή μετά τον διαδερμικό καθετηριασμό, συνεχίζει να αποδίδει όπως αναμένεται και δεν σχετίζεται με σοβαρά συμβάντα ασφαλείας.

#### **1.4.5 Σύνοψη δεδομένων από επιτήρηση μετά την κυκλοφορία του προϊόντος στην αγορά**

Υπάρχει ένα προληπτικό σύστημα παρακολούθησης (PMS) και η εξέταση όλων των καταγγελιών ολοκληρώνεται σε μηνιαία βάση και σε συμμόρφωση με τις εσωτερικές διαδικασίες κατασκευής. Τα δεδομένα καταγγελιών αναλύθηκαν κατά το χρονικό διάστημα από την 1η Σεπτεμβρίου 2019 έως την 31η Αυγούστου 2024. Συνολικά, υπήρξαν 28 Αναφορές



Επαγρύπνησης Ιατροτεχνολογικών Προϊόντων (MDV) και 476 αναφορές καταγγελιών πελατών που υποβλήθηκαν στον κατασκευαστή. Από τις 28 αναφορές MDV, 27 σχετίζονταν με ανεπιθύμητα συμβάντα και μία με δυσλειτουργία του τεχνολογικού προϊόντος. Υπήρξαν δύο θάνατοι κατά τη διάρκεια της περιόδου αναφοράς, αλλά κανένας από τους αναφερόμενους θανάτους δεν κρίθηκε ότι σχετίζεται με το εν λόγω ιατροτεχνολογικό προϊόν. Από τις 476 καταγγελίες που υποβλήθηκαν στον κατασκευαστή, οι πιο συχνές αιτίες καταγγελιών ήταν δυσκολίες στην έκπτυξη (146 συμβάντα, ποσοστό συμβάντων 0,0142%). Η κατάσταση αστοχίας συμβάντων απόσυρσης είναι η δεύτερη πιο συχνή με ποσοστό 0,0126% (130 συμβάντα).

Το σύστημα σύγκλεισης αγγείων FemoSeal™ έχει περισσότερες από 1.030.136 πωλήσεις παγκοσμίως και 827.843 στον Ευρωπαϊκό Οικονομικό Χώρο. Η υπολογισμένη συχνότητα καταγγελιών βάσει των παγκόσμιων πωλήσεων ανέρχεται στο 0,046%. Το συνολικό ποσοστό καταγγελιών από πελάτες είναι πολύ χαμηλό. Δεν εντοπίστηκαν νέοι κίνδυνοι που δεν περιλαμβάνονται στις οδηγίες χρήσης και στην τεκμηρίωση κινδύνου.

Τα ποσοστά εμφάνισης των ανεπιθύμητων ενεργειών παρουσιάζονται στον **Πίνακα 1.2**. Δεν εντοπίστηκαν νέοι μη αναμενόμενοι, αναδυόμενοι ή μη αποδεκτοί κίνδυνοι μέσω των καταγγελιών. Δεν υπήρξαν σημαντικές αυξήσεις στη συχνότητα ή τη βαρύτητα των γνωστών ανεπιθύμητων ενεργειών.

#### 1.4.6 Γενική σύνοψη της κλινικής απόδοσης και ασφάλειας

Το FemoSeal™ VCS ενδείκνυται για χρήση στη σύγκλειση της διάτρησης της κοινής μηριαίας αρτηρίας (αρτηριοτομή) σε ασθενείς που έχουν υποβληθεί σε διαδερμικό καθετηριασμό με χρήση επεμβατικού θηκαριού 7F (2,33 mm) ή μικρότερου. Αυτή η κλινική αξιολόγηση βασίζεται σε μια ολοκληρωμένη ανάλυση των διαθέσιμων κλινικών δεδομένων και της βιβλιογραφίας πριν και μετά την κυκλοφορία του προϊόντος στην αγορά που σχετίζονται με την προοριζόμενη χρήση του FemoSeal™ VCS.

Διενεργήθηκε μια ολοκληρωμένη ανασκόπηση της δημοσιευμένης βιβλιογραφίας που καλύπτει το χρονικό διάστημα από την 1η Σεπτεμβρίου 2019 έως την 31η Αυγούστου 2024. Το σύνολο των στοιχείων περιελάμβανε 29 μελέτες για το FemoSeal™ VCS. Από τα στοιχεία που παρέχονται στην κλινική αξιολόγηση εξάγεται το συμπέρασμα ότι, όταν χρησιμοποιείται όπως ενδείκνυται, το εξεταζόμενο ιατροτεχνολογικό προϊόν είναι ασφαλές και αποτελεσματικό και ότι τυχόν κίνδυνοι ή ανεπιθύμητες παρενέργειες, οι οποίες ενδέχεται να σχετίζονται με το ιατροτεχνολογικό προϊόν υπό κανονικές συνθήκες χρήσης, αποτελούν αποδεκτούς κινδύνους σε σύγκριση με τα οφέλη για τον ασθενή. Τα αποτελέσματα απόδοσης για τα εξεταζόμενα ιατροτεχνολογικά προϊόντα συνάδουν με τα αναμενόμενα για τον συγκεκριμένο τύπο ιατροτεχνολογικού προϊόντος όταν χρησιμοποιείται όπως προβλέπεται.

Τα δυνητικά ανεπιθύμητα συμβάντα που σχετίζονται με τη χρήση του FemoSeal™ VCS περιλαμβάνουν τα ανεπιθύμητα συμβάντα που αναφέρονται συνήθως με εναλλακτικά μέσα

σύγκλεισης αρτηριοτομής, π.χ. αιμορραγία και αιμάτωμα. Συνολικά, τα ποσοστά εμφάνισης για τα ανεπιθύμητα συμβάντα που αναφέρθηκαν με τη χρήση του FemoSeal™ VCS είναι παρόμοια με τα ποσοστά που αναφέρονται με χειροκίνητη συμπίεση και παρόμοια ιατροτεχνολογικά προϊόντα σύγκλεισης αγγείων. Συγκεκριμένα, για αιμορραγία και αιμάτωμα, τα αναφερόμενα ποσοστά για το FemoSeal™ VCS είναι μικρότερα από τα αναφερόμενα ποσοστά για παρόμοια ιατροτεχνολογικά προϊόντα σύγκλεισης αγγείων. Καθένα από τα αναφερόμενα ανεπιθύμητα συμβάντα, από τη δημοσιευμένη βιβλιογραφία και την παρακολούθηση μετά την κυκλοφορία του προϊόντος στην αγορά, είχαν εντοπιστεί στο παρελθόν (βλ. **Ενότητα 1.3**).

Τα υφιστάμενα δεδομένα σχετικά με την κλινική ασφάλεια και τις επιδόσεις του FemoSeal VCS υποδεικνύουν ότι τα οφέλη για τον ασθενή από τη χρήση αυτού του ιατροτεχνολογικού προϊόντος σύγκλεισης αγγείων υπερτερούν των πιθανών κινδύνων, κατά τη χρήση σύμφωνα με τις Οδηγίες χρήσης.

Όπως υποδεικνύεται στις προηγούμενες ενότητες ανωτέρω, τα δεδομένα που παρέχονται για το FemoSeal™ VCS καταδεικνύουν τη συνοχή μεταξύ των δεδομένων που σχετίζονται με το ιατροτεχνολογικό προϊόν που βρίσκεται υπό αξιολόγηση (π.χ. χρήση του ιατροτεχνολογικού προϊόντος, αποτελέσματα ασφάλειας, κλινικές επιδόσεις και κλινικά οφέλη), τις αναγνωρισμένες ισοδύναμα ιατροτεχνολογικά προϊόντα και των δεδομένων που σχετίζονται με παρόμοια ιατροτεχνολογικά προϊόντα που αναφέρονται στην τρέχουσα εξέλιξη της τεχνολογίας.

Η ανάλυση διασταύρωσης δεδομένων ασφάλειας δεν εντόπισε κενά μεταξύ των ακολούθων:

- Δεδομένων που αναφέρονται στις τελευταίες εξελίξεις στην τεχνολογία
- Δεδομένων ειδικών για το ιατροτεχνολογικό προϊόν υπό αξιολόγηση
- Δεδομένων που αναφέρονται στο(στα) αρχείο(-α) διαχείρισης κινδύνου
- Δεδομένων που αναφέρονται στην επισήμανση ή/και στις οδηγίες χρήσης (δηλ. αναφέρονται οι υπολειπόμενοι κίνδυνοι που πρέπει να γνωστοποιούνται στον χρήστη).

Η κλινική ασφάλεια έχει αποδειχθεί από τα χαμηλά ποσοστά επιπλοκών που εντοπίζονται στην δημοσιευμένη, αξιολογημένη από ομότιμους κλινική βιβλιογραφία, τις κλινικές μελέτες που χρηματοδοτούνται από την εταιρεία, την ανασκόπηση των δεδομένων μετά την κυκλοφορία του προϊόντος στην αγορά σε συνδυασμό με την απουσία αποσύρσεων από την αγορά. Δεν εντοπίστηκαν προβληματισμοί σχετικά με τις επιδόσεις. Στη βιβλιογραφία που ανασκοπήθηκε περιλαμβανόταν η χρήση του FemoSeal™ VCS η οποία ήταν σύμφωνη με την προβλεπόμενη χρήση του κατασκευαστή.

### 1.5 Πιθανές διαγνωστικές ή θεραπευτικές εναλλακτικές

Η χειροκίνητη συμπίεση χρησιμοποιείται παραδοσιακά για την επίτευξη αιμόστασης στο σημείο της αρτηριοτομής μετά από αγγειακούς καθετηριασμούς. Η χειροκίνητη συμπίεση έχει συσχετιστεί με ακινητοποίηση του ασθενούς για μεγάλα χρονικά διαστήματα (έως και 8 ώρες μετά από μια επέμβαση) και με σημαντική δυσφορία και παρατεταμένη νοσηλεία. Μια πρόσφατη συστηματική ανασκόπηση έδειξε ότι ο διάμεσος χρόνος για την επίτευξη αιμόστασης με χειροκίνητη συμπίεση ήταν 20,8 λεπτά.<sup>1</sup>

Στις εναλλακτικές λύσεις για τη χειροκίνητη συμπίεση συμπεριλαμβάνεται η χρήση εξωτερικών αιμοστατικών ιατροτεχνολογικών προϊόντων που εφαρμόζουν μηχανική συμπίεση στο σημείο της αρτηριοτομής. Τα προϊόντα αυτά δεν μειώνουν τον χρόνο επίτευξης αιμόστασης ή τον χρόνο έως το περιπατητικό στάδιο, αλλά μειώνουν τις απαιτήσεις σε προσωπικό, αντικαθιστώντας τη χειροκίνητη συμπίεση με μηχανική συμπίεση. Τα ποσοστά ανεπιθύμητων συμβάντων που σχετίζονται με τη χρήση μηχανικής συμπίεσης είναι παρόμοια με αυτά της χειροκίνητης συμπίεσης.

Τα ιατροτεχνολογικά προϊόντα σύγκλεισης αγγείων, όπως το FemoSeal™ VCS, έχουν σχεδιαστεί για σύγκλειση της αρτηριοτομής. Στόχος τους είναι να μειώσουν τον χρόνο επίτευξης αιμόστασης και να επιτρέψουν την ταχύτερη μετάβαση στο περιπατητικό στάδιο. Μια πρόσφατη συστηματική ανασκόπηση σε 13 ιατροτεχνολογικά προϊόντα που διατίθενται στο εμπόριο διαπίστωσε ότι ο διάμεσος χρόνος για την επίτευξη αιμόστασης με ιατροτεχνολογικό προϊόν σύγκλεισης αγγείων ήταν 5,4 λεπτά. Ο διάμεσος χρόνος αιμόστασης για τα μεμονωμένα ιατροτεχνολογικά προϊόντα σύγκλεισης αγγείων κυμαινόταν από 1 λεπτό (FemoSeal™ VCS) έως 14 λεπτά, με την πλειονότητα των προϊόντων να κυμαίνεται μεταξύ 4 και 10 λεπτών.<sup>1</sup>

Τα συχνά αναφερόμενα ανεπιθύμητα συμβάντα που σχετίζονται με τη σύγκλειση του σημείου της αρτηριοτομής, με χειροκίνητες συμπίεσεις, εξωτερικά αιμοστατικά ιατροτεχνολογικά προϊόντα ή ιατροτεχνολογικά προϊόντα σύγκλεισης αγγείων περιλαμβάνουν αιμάτωμα, αιμορραγία στο σημείο πρόσβασης, ψευδοανεύρυσμα, αρτηριοφλεβικό συρίγγιο και μόλυνση. Η ίδια συστηματική ανασκόπηση (34 τυχαιοποιημένες ελεγχόμενες δοκιμές, 14.401 ασθενείς) διαπίστωσε ότι τα ποσοστά ανεπιθύμητων συμβάντων ήταν παρόμοια μεταξύ της χειροκίνητης συμπίεσης και της χρήσης ιατροτεχνολογικών προϊόντων σύγκλεισης αγγείων, με την εξαίρεση ότι η αιμορραγία έτεινε να είναι λίγο υψηλότερη με ιατροτεχνολογικά προϊόντα σύγκλεισης αγγείων.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

### 1.6 Προτεινόμενο προφίλ χρηστών και εκπαίδευση

Οι προβλεπόμενοι χρήστες του FemoSeal™ Vascular Closure System είναι ιατροί με εκπαίδευση που τους επιτρέπει τη διεξαγωγή αρτηριακής πρόσβασης και σύγκλεισης για ενδοαγγειακές επεμβάσεις μέσω της κοινής μηριαίας αρτηρίας και έχουν συμμετάσχει σε ένα πρόγραμμα εκπαίδευσης ιατρών της Terumo Medical Corporation FemoSeal™.

### 1.7 Σχετικά εναρμονισμένα και κοινά πρότυπα

| Κωδικός προτύπου | Τρέχον έτος συμμόρφωσης/Αναθ. | Περιγραφή                                                                                                                                |
|------------------|-------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070        | 2014/AMD1:2018                | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070     | 2014/A1:2018                  | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| Οδηγία FDA       | 20 Μαΐου 2021                 | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052       | 2015                          | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213       | 2017                          | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503       | 2020                          | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182       | 2019                          | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |
| EN ISO 13485     | 2016/A11:2021                 | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 13485        | 2016                          | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |

| Κωδικός<br>προτύπου | Τρέχον έτος<br>συμμόρφωσης/Αναθ. | Περιγραφή                                                                                                                                                                   |
|---------------------|----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14644-1         | 2015                             | Cleanrooms and associated controlled environments<br>— Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1      | 2015                             | Cleanrooms and associated controlled environments<br>— Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2         | 2015                             | Cleanrooms and associated controlled environments<br>— Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2      | 2015                             | Cleanrooms and associated controlled environments<br>— Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3         | 2019                             | Cleanrooms and associated controlled environments<br>— Part 3: Test methods                                                                                                 |
| EN ISO 14644-3      | 2019                             | Cleanrooms and associated controlled environments<br>— Part 3: Test methods                                                                                                 |
| ISO 14698-1         | 2003                             | Cleanrooms and associated controlled environments<br>— Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1      | 2003                             | Cleanrooms and associated controlled environments<br>— Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2         | 2003/TC1:2004                    | Cleanrooms and associated controlled environments<br>— Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| EN ISO 14698-2      | 2003/TC 1:2004                   | Cleanrooms and associated controlled environments<br>— Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| USP <788>           | Δ/Υ                              | PARTICULATE MATTER IN INJECTIONS                                                                                                                                            |

| Κωδικός προτύπου          | Τρέχον έτος συμμόρφωσης/Αναθ. | Περιγραφή                                                                                                            |
|---------------------------|-------------------------------|----------------------------------------------------------------------------------------------------------------------|
| Φαρμακοποιία<br>ΕΕ 2.9.19 | Δ/Υ                           | Particulate Contamination: Sub-Visible Particles                                                                     |
| IEC 62366-1               | 2015                          | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN 62366-1                | 2015                          | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN ISO 14971              | 2019/A11:2021                 | Medical devices — Application of risk management to Medical devices                                                  |
| ISO 14971                 | 2019                          | Medical devices — Application of risk management to Medical devices                                                  |
| ASTM F1980                | 2016                          | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1            | 2020                          | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1               | 2018                          | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2            | 2006                          | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2               | 2006                          | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3            | 2014                          | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3               | 2014                          | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4            | 2017                          | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4               | 2017                          | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |

| Κωδικός προτύπου | Τρέχον έτος συμμόρφωσης/Αναθ. | Περιγραφή                                                                                                                                  |
|------------------|-------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-5   | 2009                          | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                                         |
| ISO 10993-5      | 2009                          | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                                         |
| EN ISO 10993-6   | 2016                          | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| ISO 10993-6      | 2016                          | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| EN ISO 10993-10  | 2023                          | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| ISO 10993-10     | 2021                          | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| EN ISO 10993-11  | 2018                          | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| ISO 10993-11     | 2017                          | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| EN ISO 10993-12  | 2021                          | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| ISO 10993-12     | 2021                          | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| EN ISO 10993-17  | 2009                          | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17     | 2002                          | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18     | 2020/A1:2022                  | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |



| Κωδικός προτύπου | Τρέχον έτος συμμόρφωσης/Αναθ. | Περιγραφή                                                                                                                                                                    |
|------------------|-------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-18  | 2020/A1:2022                  | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-23  | 2021                          | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23     | 2021                          | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382       | 2018                          | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756        | 2017                          | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>         | Δ/Y                           | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>        | Δ/Y                           | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72   | 2019                          | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135     | 2014/A1:2019                  | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135        | 2014/A1:2018                  | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7   | 2008/A1:2022                  | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |



| Κωδικός<br>προτύπου | Τρέχον έτος<br>συμμόρφωσης/Αναθ. | Περιγραφή                                                                                                                                                       |
|---------------------|----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-7         | 2008/A1:2019                     | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                               |
| EN 556-1            | 2024                             | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices |
| EN ISO 11737-1      | 2018/A1:2021                     | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11737-1         | 2018/A1:2021                     | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| EN ISO 11138-1      | 2017                             | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-1         | 2017                             | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| EN ISO 11138-2      | 2017                             | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 11138-2         | 2017                             | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| EN ISO 15223-1      | 2016                             | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| ISO 15223-1         | 2016                             | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| EN 1041             | 2008/A1:2013                     | Information supplied by the manufacturer of medical devices                                                                                                     |

| Κωδικός<br>προτύπου | Τρέχον έτος<br>συμμόρφωσης/Αναθ. | Περιγραφή                                                                                                                                                                  |
|---------------------|----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 11607-1      | 2020/A1:2023                     | Packaging for Terminally Sterilized Medical Devices<br>– Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                 |
| ISO 11607-1         | 2019/A1:2023                     | Packaging for Terminally Sterilized Medical Devices<br>– Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                 |
| EN ISO 11607-2      | 2020/A1:2023                     | Packaging for Terminally Sterilized Medical Devices<br>– Part 2: Validation requirements for forming, sealing, and assembly processes                                      |
| ISO 11607-2         | 2019/A1:2023                     | Packaging for Terminally Sterilized Medical Devices<br>– Part 2: Validation requirements for forming, sealing, and assembly processes                                      |
| ASTM D4169          | 2016                             | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M   | 2016                             | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825          | 2018                             | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096          | 2011 (R 2019)                    | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M       | 2015                             | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24        | 2021                             | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3         | 2020                             | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |

| Κωδικός προτύπου | Τρέχον έτος συμμόρφωσης/Αναθ. | Περιγραφή                                                                                                                                                                                          |
|------------------|-------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-8      | 2020                          | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                                                     |
| MDCG 2020-7      | 2020                          | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                                                  |
| MDCG 2020-6      | 2020                          | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                                               |
| MDCG 2019-9 v1   | 2022                          | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                           |
| MDCG 2019-8 v2   | 2020                          | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                 |
| MDCG 2020-15     | 2020                          | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                           |
| MDCG 2021-11     | 2021                          | Guidance on Implant Card – ‘Device types’                                                                                                                                                          |
| MDCG 2021-19     | 2021                          | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                            |
| MDCG 2018-1 v4   | 2021                          | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                     |
| MDCG 2019-2      | 2019                          | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                 |
| MDCG 2019-1      | 2019                          | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                 |
| MDCG 2018-7      | 2018                          | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro |

| Κωδικός προτύπου      | Τρέχον έτος συμμόρφωσης/Αναθ. | Περιγραφή                                                                                                                                                                                     |
|-----------------------|-------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                       |                               | Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR))                                                                                                                                    |
| MDCG 2018-6           | 2018                          | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746   |
| MDCG 2018-4           | 2018                          | MDCG 2018-4 Annex: UDI database Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                                  |
| MDCG 2018-3 v1        | 2020                          | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25          | 2021                          | Regulation (EU) 2017/745 - application of MDR requirements to ‘legacy devices’ and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2.12-2 Αναθ. 2 | 2012                          | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                        |

## 2.0 ΒΙΒΛΙΟΓΡΑΦΙΑ

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### 3.0 ΙΣΤΟΡΙΚΟ ΑΝΑΘΕΩΡΗΣΕΩΝ

| Αριθμός αναθεώρησης SSCP    | Ημερομηνία έκδοσης | Περιγραφή αλλαγής                                                                        | Αναθεώρηση επικυρωμένη από τον Κοινοποιημένο Οργανισμό                                                                                                                                                                                                                                                                                                                                                                                                        |
|-----------------------------|--------------------|------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022                | 20 Ιανουαρίου 2023 | Αρχική έκδοση, με πιστοποίηση MDR CE                                                     | <p><input checked="" type="checkbox"/> Ναι</p> <p>Γλώσσα επικύρωσης:<br/>English</p> <p><input type="checkbox"/> Όχι (ισχύει μόνο για εμφυτεύσιμα ιατροτεχνολογικά προϊόντα κατηγορίας Πα ή ορισμένα εμφυτεύσιμα ιατροτεχνολογικά προϊόντα κατηγορίας ΙΙβ (MDR, άρθρο 52 (4) 2η παράγραφος) για τα οποία το SSCP δεν έχει επικυρωθεί ακόμη από τον κοινοποιημένο οργανισμό)</p> <p><input type="checkbox"/> Άλλο (διευκρίνιση):</p>                           |
| SSCP-AS-2023 – Αναθεώρηση 1 | 15 Μαρτίου 2024    | Επικαιροποιήθηκε για την περίοδο από την 1η Ιανουαρίου 2019 έως την 31η Δεκεμβρίου 2023. | <p><input checked="" type="checkbox"/> Ναι</p> <p>Γλώσσα επικύρωσης:<br/>English</p> <p><input type="checkbox"/> Όχι (ισχύει μόνο για εμφυτεύσιμα ιατροτεχνολογικά προϊόντα κατηγορίας Πα ή ορισμένα εμφυτεύσιμα ιατροτεχνολογικά προϊόντα κατηγορίας ΙΙβ (MDR, ιατροτεχνολογικά προϊόντα άρθρο 52 (4) 2η παράγραφος) για τα οποία το SSCP δεν έχει επικυρωθεί ακόμη από τον κοινοποιημένο οργανισμό)</p> <p><input type="checkbox"/> Άλλο (διευκρίνιση):</p> |
| SSCP-FS-2024 Αναθεώρηση 1   |                    | Επικαιροποιήθηκε για την περίοδο από την 1η Σεπτεμβρίου 2019 έως                         | <p><input type="checkbox"/> Ναι</p> <p>Γλώσσα επικύρωσης:<br/>English</p>                                                                                                                                                                                                                                                                                                                                                                                     |



|                                                 |                          |                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|-------------------------------------------------|--------------------------|------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                 |                          | <div>την 31η Αυγούστου 2024.</div>                               | <div> <input type="checkbox"/> Όχι (ισχύει μόνο για εμφυτεύσιμα ιατροτεχνολογικά προϊόντα κατηγορίας Πα ή ορισμένα εμφυτεύσιμα ιατροτεχνολογικά προϊόντα κατηγορίας Πβ (MDR, ιατροτεχνολογικά προϊόντα άρθρο 52 (4) 2η παράγραφος) για τα οποία το SSCP δεν έχει επικυρωθεί ακόμη από τον κοινοποιημένο οργανισμό)                 </div> <div> <input type="checkbox"/> Άλλο (διευκρίνιση):                 </div>                                                                                                                |
| <div>SSCP-FS-2024</div> <div>Αναθεώρηση 2</div> | <div>June 20, 2025</div> | <div>Αναθεωρήθηκε με βάση ερωτήματα της NSAI για επικύρωση</div> | <div> <input checked="" type="checkbox"/> Ναι                     <div>Γλώσσα επικύρωσης: English</div> </div> <div> <input type="checkbox"/> Όχι (ισχύει μόνο για εμφυτεύσιμα ιατροτεχνολογικά προϊόντα κατηγορίας Πα ή ορισμένα εμφυτεύσιμα ιατροτεχνολογικά προϊόντα κατηγορίας Πβ (MDR, ιατροτεχνολογικά προϊόντα άρθρο 52 (4) 2η παράγραφος) για τα οποία το SSCP δεν έχει επικυρωθεί ακόμη από τον κοινοποιημένο οργανισμό)                 </div> <div> <input type="checkbox"/> Άλλο (διευκρίνιση):                 </div> |

## Sažetak o sigurnosnoj i kliničkoj učinkovitosti

### Sustav FemoSeal™ Vascular Closure System

|                                                              |                                                                                              |
|--------------------------------------------------------------|----------------------------------------------------------------------------------------------|
| <b>Proizvođač</b>                                            | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 SAD          |
| <b>Jedinstveni registracijski broj<br/>proizvođača (SRN)</b> | US-MF-000019594                                                                              |
| <b>Predstavnik uprave / PRRC</b>                             | Kimberly Feitl<br>Vice President, Quality                                                    |
| <b>Osnovni UDI-DI</b>                                        | 38970FS79                                                                                    |
| <b>EMDN broj</b>                                             | C900199 – sustavi za hemostazu – ostalo                                                      |
| <b>Razred opreme</b>                                         | Razred III                                                                                   |
| <b>Prva godina koje je proizvod dobio<br/>oznaku CE</b>      | 2005.                                                                                        |
| <b>Predstavnik u EU-u</b>                                    | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgija<br>SRN: BE-AR-000001433 |
| <b>Prijavljeno tijelo</b>                                    | NSAI<br>CE 0050                                                                              |

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Ovaj sažetak o sigurnosnoj i kliničkoj učinkovitosti (SSCP) pruža javni pristup ažuriranom sažetku glavnih aspekata sigurnosti i kliničke učinkovitosti sustava FemoSeal™ Vascular Closure System (VCS).

Sažetak o sigurnosnoj i kliničkoj učinkovitosti proizvoda namijenjen korisnicima / zdravstvenim djelatnicima naveden je u nastavku, u **dijelu 1.0**.

## **1.0 SAŽETAK ZA KORISNIKE / ZDRAVSTVENE DJELATNIKE**

Sažetak o sigurnosnoj i kliničkoj učinkovitosti nije namijenjen kao zamjena za Upute za uporabu kao glavni dokument da bi se osigurala sigurna uporaba proizvoda niti je namijenjen za pružanje dijagnostičkih ili terapijskih prijedloga predviđenim korisnicima ili pacijentima. Sažetak o sigurnosnoj i kliničkoj učinkovitosti nije namijenjen kao zamjena za obavezne podatke na karticama implantata ili u drugim obaveznim dokumentima.

### **1.1 Namjena proizvoda**

#### **1.1.1 Namjena**

Sustav FemoSeal™ Vascular Closure System medicinski je proizvod namijenjen za zatvaranje arterijske punkcije nakon perkutane kateterizacije kroz zajedničku femoralnu arteriju.

#### **1.1.2 Indikacije za uporabu**

Sustav FemoSeal™ Vascular Closure System indiciran je za uporabu kod zatvaranja punkcije (arteriotomije) zajedničke femoralne arterije u pacijenata kod kojih je provedena perkutana kateterizacija s pomoću uvedne ovojnice debljine 7 F (2,33 mm) ili manje.

#### **1.1.3 Kontraindikacije i/ili ograničenja**

Sustav FemoSeal™ Vascular Closure System kontraindiciran je u pacijenata s arteriotomijama kod kojih su upotrijebljene uvedne ovojnice ili proizvodi veći od 7 F (2,33 mm).

#### **1.1.4 Ciljne populacije**

Sigurnost i djelotvornost sustava FemoSeal™ Vascular Closure System utvrđena je u pacijenata u dobi od 18 godina i starijih koji su bili podvrgnuti perkutanoj kateterizaciji uporabom uvedne ovojnice veličine 7 F (2,33 mm) ili manje.

#### **1.1.5 Posebne populacije pacijenata**

Sigurnost i učinkovitost sustava FemoSeal™ Vascular Closure System nije utvrđena u sljedećim populacijama pacijenata:

- pacijenti s već postojećom autoimunom bolesti
- pacijenti koji se podvrgavaju terapijskoj trombolizi
- pacijenti s klinički značajnim bolestima perifernih krvnih žila
- pacijenti s nekontroliranom hipertenzijom (> 220 mmHg sistolički ili > 110 mmHg dijastolički)

- pacijenti s poremećajima krvarenja, uključujući trombocitopeniju (broj trombocita < 100.000), ili anemijom (Hgb < 10 mg/dl)
- pacijenti s unutarnjim lumenom zajedničke femoralne arterije manjim od 5 mm
- pacijenti s oštećenjem bubrega i/ili jetre
- pacijenti s drugim relevantnim komorbiditetima
- populacija sa specifičnim rasnim i/ili etničkim podrijetlom
- pacijenti s infarktom miokarda unutar 72 sata
- pacijenti s vaskularnim presadkom ili stentom na mjestu punkcije
- trudnice i dojilje
- pacijenti mlađi od 18 godina.

#### 1.1.6 Predviđeni korisnici

Predviđeni su korisnici sustava FemoSeal™ Vascular Closure System liječnici koji su završenom obukom kvalificirani za obavljanje arterijskog pristupa i zatvaranja u okviru endovaskularnih zahvata kroz zajedničku femoralnu arteriju te koji su sudjelovali u programu obuke za liječnike za FemoSeal™ društva Terumo Medical Corporation.

## 1.2 Opis proizvoda

### 1.2.1 Opis proizvoda

Sustav FemoSeal™ Vascular Closure System, koji proizvodi društvo Terumo Medical Corporation (TMC), resorptivni je proizvod za zatvaranje krvnih žila namijenjen za postizanje hemostaze femoralne arterije nakon perkutane kateterizacije kroz zajedničku femoralnu arteriju.

Elementi za zatvaranje sustava FemoSeal™ sastoje se od dvaju resorptivnih polimernih diskova, unutarnje brtve i vanjskog diska za zaključavanje koji su međusobno povezani resorbirajućim multifilamentom, čime se mehanički zatvara arteriotomija (pogledajte **sliku 1.1** i **sliku 1.2**).

Nakon postavljanja kroz ovojnicu konusnog kućišta, vanjski disk za zaključavanje nabija se na multifilamentnu osovinu, što dovodi do mehaničkog zatvaranja mjesta punkcije između unutarnjeg i vanjskog diska za zaključavanje. Unutarnja brtva i vanjski disk za zaključavanje drže se na mjestu trenjem na multifilamentnoj osovinu. Hemostaza se postiže mehaničkim sredstvima. Elementi za zatvaranje razgrađuju se hidrolizom.

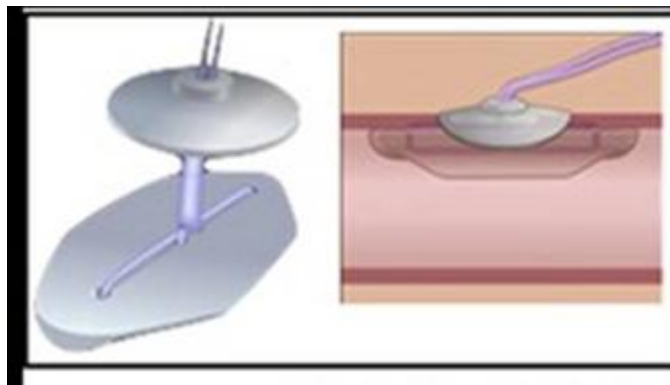
Komponente za zatvaranje koje se implantiraju, unutarnja brtva i vanjski disk za zaključavanje razgrađuju se tijekom osamnaest (18) mjeseci, dok se procjenjuje da se multifilament razgrađuje

i resorbira hidrolizom u okolna tkiva nakon od dvije (2) do tri (3) godine. Mogućnost implantiranih komponenti za zatvaranje za održavanje kompresije na arteriotomiji ispitana je do osam (8) sati. Proizvodi razgrađivanja metaboliziraju se i izlučuju urinom ili se preko pluća izdišu kao ugljikov dioksid. Nisu zapaženi učinci nakupljanja u ispitivanjima na životinjama. Dodatne komponente sustava FemoSeal™ koje će doći u dodir sa živim tkivom ili krvlju tijekom zahvata su ovojnica konusnog kućišta, dilatator, cijev za nabijanje, potiskivač i žica vodicica.

**Slika 1.1 Unutarnja brtva i vanjski disk za zaključavanje**



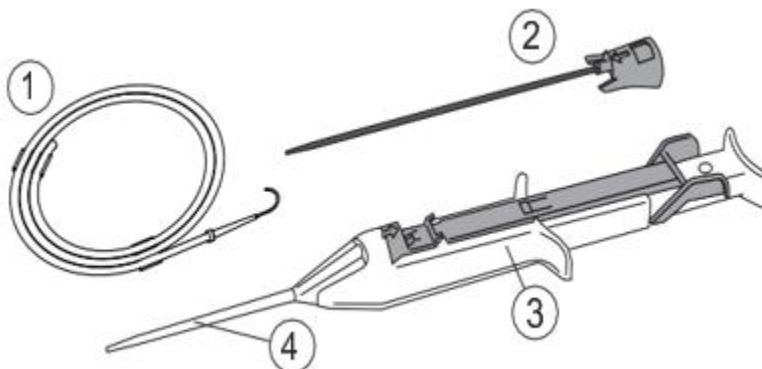
**Slika 1.2 Postavljena unutarnja brtva i vanjski disk za zaključavanje**



Jedinica FemoSeal™ pakirana je zajedno s dilatatorom i žicom vodicicom vanjskog promjera 0,038" (0,97 mm), duljine 27,5" (70 cm) i elementom za izravnavanje oblika slova J, pogledajte **sliku 1.3** u nastavku. Žica vodicica nalazi se unutar polietilenske cijevi. Svi su dijelovi zapakirani u fiksnu papirnatu pliticu. Pakiranje uključuje i karticu implantata za pacijenta. Sustav FemoSeal™ Vascular Closure System ne zahtijeva dodatni pribor da bi proizvod funkcionirao kako je predviđeno, a proizvod je namijenjen samo za uporabu s dilatatorom i žicom vodicicom koji se nalaze u pakiranju proizvoda.



Slika 1.3 Jedinica sustava FemoSeal™ VCS sa žicom vodilicom i dilatatorom



## 1.2.2 Sirovine i komponente

U tablici 1.1 u nastavku navedene su komponente sustava FemoSeal™ VCS.

Tablica 1.1 Sirovine i komponente sustava FemoSeal™ VCS

| Broj dijela | Opis                                                                                       |                                                                          | Materijal                                                                                                                                                                       |
|-------------|--------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1           | Žica vodilica od 0,038" (0,97 mm) s elementom za izravnavanje žice vodilice oblika slova J |                                                                          | Žica vodilica: nehrđajući čelik 304<br>Element za izravnavanje oblika slova J: Polipropilen, ljubičasti pigment<br>Kopča: polietilen<br>Cijev: polietilen                       |
| 2           | Dilatator FemoSeal™                                                                        |                                                                          | Priključak: tetrahidrofuran, plavi pigment, polibutilen-tereftalat (PBT)<br>Cijev: polietilen visoke gustoće (HDPE), crni pigment<br>Mazivo: Silikonski Dow Corning 360         |
| 3/4         | Jedinica FemoSeal                                                                          | RD7 oblikovan kalupom – unutarnja brtva i vanjski disk za zaključavanje* | Kopolimer između glikolida, trimetil-karbonata, ε-kaprolaktona i TMP-a: trimetilolpropan (inicijator)                                                                           |
|             |                                                                                            | Multifilament*                                                           | Segmentirani kopolimer između L,L-laktida, trimetil-karbonata, ε-kaprolaktona i 1,3 propandiola (inicijator)<br>Premaz je kopolimer između glikolida, ε-kaprolaktona i L-lizina |

|  |  |                              |                                                    |
|--|--|------------------------------|----------------------------------------------------|
|  |  | Cijev za nabijanje           | Polipropilen                                       |
|  |  | Potiskivač                   | Nehrđajući čelik 304V                              |
|  |  | Klizač                       | Polibutetilen-tereftalat (PBT)                     |
|  |  | Kućište                      | Polibutetilen-tereftalat (PBT)                     |
|  |  | Gumb                         | Polibutetilen-tereftalat (PBT)                     |
|  |  | Poklopac gumba               | Polioksimetilen (POM)/poliacetal<br>kopolimer      |
|  |  | Čahura                       | Polibutetilen-tereftalat (PBT)                     |
|  |  | Odstojnik                    | Polibutetilen-tereftalat (PBT)                     |
|  |  | Konus                        | Polipropilen                                       |
|  |  | Poklopac kućišta             | Polibutetilen-tereftalat (PBT)                     |
|  |  | Sigurnosna kopča             | Polibutetilen-tereftalat (PBT), plavi<br>pigment   |
|  |  | Poklopac čahure              | Polibutetilen-tereftalat (PBT)                     |
|  |  | Brтва cijevi                 | Silikon shore A 70                                 |
|  |  | Brтва kućišta                | Silikonska shore A 50                              |
|  |  | Opruga                       | Nehrđajući čelik 302                               |
|  |  | Ovojnica konusnog<br>kućišta | Polipropilen<br>Silikon Dow Corning 360, heksanski |

\* Ugradivi dio proizvoda; komponente za ugradnju sigurne su za MR

Sustav FemoSeal™ VCS steriliziran je etilen-oksidom (EO) i medicinski je proizvod za jednokratnu uporabu. Sustav FemoSeal™ VCS konstruiran je tako da se ne može ponovno upotrijebiti.

### **Način funkcioniranja**

Sustav FemoSeal™ VCS potiče mehaničku hemostazu postavljanjem ugradivih elemenata za zatvaranje unutar i izvan zajedničke femoralne arterije. Mehanizam kojim se sprječava krvarenje omogućuju unutarnja brtva koja zatvara mjesto punkcije i vanjski disk za zaključavanje koji drži unutarnju brtvu na mjestu.

### 1.2.3 Klinička korist

Sustav FemoSeal™ VCS pruža sljedeće kliničke koristi u odnosu na zatvaranje krvnih žila nakon punkcije zajedničke femoralne arterije:

- Smanjenje vremena za postizanje hemostaze<sup>1</sup>
- Smanjenje vremena za postizanje pokretljivosti<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015.). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

### 1.2.4 Prethodne generacije ili varijante

- Prva verzija sustava FemoSeal™ VCS (#11200) prodavala se na europskom tržištu tijekom 2005. godine i dijela 2006.
- Trenutačni sustav FemoSeal™ VCS (#11202), s poboljšanim sustavom uvođenja, nalazi se na tržištu od 28. ožujka 2006.

### 1.2.5 Pribor namijenjen za upotrebu u kombinaciji s proizvodom

Jedinica FemoSeal™ pakirana je zajedno s dilatatorom, žicom vodilicom vanjskog promjera 0,038" (0,97 mm) i duljine 27,5" (70 cm) te elementom za izravnavanje oblika slova J. Žica vodilica dodatna je oprema za jedinicu FemoSeal™. Element za izravnavanje oblika slova J sastavni je dio žice vodilice, dok je dilatator sastavni dio jedinice FemoSeal™. Žica vodilica je jedini dodatni pribor. Žica vodilica nalazi se unutar polietilenske cijevi. Svi su dijelovi zapakirani u fiksnu papirnatu pliticu. Pakiranje uključuje i karticu implantata za pacijenta. Sustav FemoSeal™ Vascular Closure System ne zahtijeva dodatni pribor da bi proizvod funkcionirao kako je predviđeno, a proizvod je namijenjen samo za uporabu s dilatatorom i žicom vodilicom koji se nalaze u pakiranju proizvoda.

### 1.2.6 Ostali uređaji i proizvodi namijenjeni za upotrebu u kombinaciji s proizvodom

Sustav FemoSeal™ VCS ne zahtijeva dodatne proizvode kako bi funkcionirao kako je predviđeno.

## 1.3 Rizici i upozorenja

### 1.3.1 Preostali rizici i neželjeni učinci

U **tablici 1.2** navedeni su poznati ili predvidljivi štetni događaji, negativne posljedice i komplikacije povezane s uporabom proizvoda FemoSeal™ VCS kao rezultat preostalih rizika. Stopa učestalosti temelji se na analizi dokumentacije o riziku i izračunava se na temelju podataka postmarketinškog nadzora od 1. rujna 2019. do 31. kolovoza 2024. Nema nepoznatih preostalih

rizika za FemoSeal™ VCS i svi su primjenjivi rizici obrađeni u Uputama za uporabu i postupku upravljanja rizicima.

**Tablica 1.2. Štetni događaji / komplikacije povezani s proizvodom FemoSeal**

| Šteta                                        | Stopa učestalosti (%) | Čimbenici za izbjegavanje                                                                                                                                              |
|----------------------------------------------|-----------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Alergijska reakcija                          | 0,0000                | Mjere i planovi za smanjenje rizika na što nižu razinu adresirani su značajkama dizajna proizvoda, proizvodnim smjernicama, označivanjem proizvoda i obukom liječnika. |
| Aneurizma                                    | 0,0000                |                                                                                                                                                                        |
| Arteriovenska fistula                        | 0,0001                |                                                                                                                                                                        |
| Gubitak krvi / krvarenje                     | 0,0280                |                                                                                                                                                                        |
| Smrt                                         | 0,0002                |                                                                                                                                                                        |
| Ekhimoz                                      | 0,0000                |                                                                                                                                                                        |
| Embolija                                     | 0,0000                |                                                                                                                                                                        |
| Reakcija na strano tijelo                    | 0,0000                |                                                                                                                                                                        |
| Hematom                                      | 0,0027                |                                                                                                                                                                        |
| Krvarenje                                    | 0,0001                |                                                                                                                                                                        |
| Infekcija                                    | 0,0002                |                                                                                                                                                                        |
| Upalna reakcija                              | 0,0000                |                                                                                                                                                                        |
| Utrnulost                                    | 0,0000                |                                                                                                                                                                        |
| Bol                                          | 0,0000                |                                                                                                                                                                        |
| Nelagoda kod pacijenta                       | 0,0004                |                                                                                                                                                                        |
| Odgadanje postupka                           | 0,0065                |                                                                                                                                                                        |
| Pseudoaneurizma                              | 0,0004                |                                                                                                                                                                        |
| Retroperitonealno krvarenje                  | 0,0002                |                                                                                                                                                                        |
| Sepsa                                        | 0,0000                |                                                                                                                                                                        |
| Tromboembolija                               | 0,0000                |                                                                                                                                                                        |
| Tromboza                                     | 0,0001                |                                                                                                                                                                        |
| Okluzija krvnih žila / ishemija donjih udova | 0,0002                |                                                                                                                                                                        |
| Perforacija žila                             | 0,0000                |                                                                                                                                                                        |
| Disekcija/laceracija krvnih žila             | 0,0003                |                                                                                                                                                                        |

### 1.3.2 Upozorenja i mjere opreza

#### Upozorenja

1. Nemojte upotrebljavati ako je pakiranje oštećeno ili ako je bilo koja sterilna barijera oštećena.
2. Nemojte upotrebljavati nakon isteka roka valjanosti jer bi biorazgradive komponente mogle biti neadekvatne za rad.
3. Nemojte upotrebljavati ako bilo koji predmet izgleda oštećen ili neispravan.
4. Uporaba sustava FemoSeal™ Vascular Closure System kod kojeg je možda došlo do bakterijske kontaminacije uvedne ovojnice ili okolnog tkiva može uzrokovati infekciju.
5. Ako postoji sumnja da je stražnja stijenka arterije probušena ili je izvršeno više od jedne arterijske punkcije, nemojte se oslanjati isključivo na sustav FemoSeal™ Vascular Closure System za postizanje arterijske hemostaze. Upotrijebite dodatnu ručnu ili mehaničku kompresiju.
6. Ako je mjesto uboda na ili distalno od bifurkacije femoralne arterije, sustav FemoSeal™ Vascular Closure System ne smije se upotrebljavati zbog rizika od pogrešnog postavljanja unutarnje brtve. Ovaj događaj može dovesti do komplikacija krvarenja i/ili poremećaja uobičajenog protoka krvi.
7. Ako na mjestu reza dolazi do stalnog arterijskog krvarenja, nemojte rezati multifilament sve dok se ne postigne hemostaza. Ako se ne postigne hemostaza, učvrstite multifilament sterilnim povojem za rane i primijenite dodatnu kompresiju dok se ne postigne hemostaza. U slučaju dugotrajnog arterijskog krvarenja može doći do znatnih komplikacija koje mogu rezultirati ozljedom ili smrću pacijenta.
8. Sustav FemoSeal™ Vascular Closure System nemojte upotrebljavati ako je mjesto uboda proksimalno u odnosu na ingvinalni ligament jer to može dovesti do retroperitonealnog hematoma.
9. Pacijenti s povećanim rizikom od krvarenja mogu pretrpjeti povećani gubitak krvi, zbog čega je potrebna transfuzija.
10. Ako se unutarnji disk odvoji, to potencijalno može uzrokovati trombozu i/ili emboliju.

#### Mjere opreza

1. Postupak ugradnje sustava FemoSeal™ Vascular Closure System moraju obaviti liječnici s odgovarajućom obukom za uporabu ovog proizvoda.
2. Snimite ograničeni femoralni angiogram ili ultrazvučno navođenu femoralnu punkciju prije postavljanja sustava FemoSeal™ Vascular Closure System.

3. Prekinite postupak ako:
  - promjer lumena zajedničke femoralne arterije je  $< 5$  mm
  - u blizini mjesta punkcije na zajedničkoj femoralnoj arteriji prisutna je stenoza i/ili znatna količina plaka
  - arterijska punkcija je na mjestu bifurkacije femoralne arterije ili distalno od nje
  - u blizini mjesta punkcije zajedničke femoralne arterije nalaze se anomalije grana ili krvnih žila.
4. Ako je prisutan hematoma, potrebno je posebno paziti da se ovojnica konusnog kućišta ispravno uvede u arteriju.
5. Koristite tehniku punkcije jedne stijenke. Nemojte probijati stražnju stijenku arterije.
6. Uvijek se pridržavajte sterilne tehnike prilikom uporabe sustava FemoSeal™ Vascular Closure System.
7. Sustav FemoSeal™ Vascular Closure System namijenjen je samo za jednokratnu uporabu i ne smije se ni na koji način ponovno sterilizirati ni upotrebljavati. Jedinica FemoSeal™ osmišljena je tako da se ne može ponovno upotrijebiti.
8. Ako tijekom postavljanja unutarnje brtve osjetite neočekivani otpor, prekinite postupak.
9. Za ispravno postavljanje unutarnje brtve ponovno postavite palac tako da se gumb može slobodno vratiti natrag.
10. Prije postavljanja vanjskog blokirajućeg diska provjerite je li vrh konusnog kućišta FemoSeal™ jedinice ispod površine kože. Vanjski disk za zaključavanje može se nenamjerno postaviti iznad razine kože u pacijenata kod koji je razdaljina između femoralne arterije i razine kože kratka.
11. Za ispravno postavljanje može biti potrebna incizija kože prije postavljanja.
12. Ako je unutarnja brtva unutar arterije, ali nije moguće potpuno pritisnuti gumb i postaviti vanjski disk za zaključavanje, može biti potreban kirurški zahvat za uklanjanje elemenata za zatvaranje FemoSeal™.
13. Ako je u roku od 18 mjeseci potrebno ponoviti punkciju iste femoralne arterije, ponovnu punkciju treba napraviti najmanje jedan centimetar proksimalno od prethodnog mjesta pristupa sa sustavom FemoSeal™ Vascular Closure System.
14. Uputite pacijenta da se pridržava liječnikovih uputa u vezi s pregledom mjesta zatvaranja.
15. Uputite pacijenta da sa sobom sljedećih 18 mjeseci nosi karticu s informacijama za pacijenta

### **Mjere opreza prilikom otpuštanja**

Prije razmatranja otpuštanja iz bolnice procijenite pacijentovo stanje u pogledu sljedećih kliničkih stanja:

1. krvarenje i/ili hematoma na mjestu zatvaranja
2. Bol prilikom hodanja.
3. Znakovi infekcije na mjestu zatvaranja.

### **1.3.3 Sigurnosne korektivne radnje**

U razdoblju od 1. rujna 2019. do 31. kolovoza 2024. poduzeta je jedna korektivna radnja na terenu vezana uz FemoSeal™ VCS.

Godine 2022. Terumo je dobrovoljno opozvao FemoSeal™ VCS zbog pritužbi u kojima su se navodili neuspjesi u procesu i testiranju puštanja serije Elktonovog proizvoda FemoSeal za mjerenje sile nabijanja i sile retrakcije. Iz Južne Koreje povučeno je ukupno 950 jedinica.

## **1.4 Klinička procjena i praćenje nakon stavljanja u promet**

**Tablica 1.3** obuhvaća popis ključnih ispitivanja uključenih za stavljanje sustava FemoSeal™ VCS u promet kao i ispitivanja nakon stavljanja u promet te aktivnosti praćenja nakon stavljanja u promet. Verzija proizvoda korištena u ispitivanju navedena je u tablici u nastavku. Prva verzija sustava FemoSeal™ VCS (#11200) bila je u prometu do 2006., dok je sljedeća verzija (#C11202) puštena u promet 2006. godine te je ono što se danas nalazi u prometu.

**Tablica 1.3 Sažetak ključnih ispitivanja**

| <b>Funkcionalna ispitivanja na životinjama prije stavljanja u promet</b>                                                                                                                                                                                                | <b>Verzija proizvoda</b> |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                    |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                    |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                    |
| <b>Prvo kliničko ispitivanje na ljudima</b>                                                                                                                                                                                                                             |                          |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                    |

| Završena klinička ispitivanja nakon stavljanja u promet                                                                         |                                 |
|---------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                      | C11202<br>(trenutačni proizvod) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                               | C11202<br>(trenutačni proizvod) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | C11202<br>(trenutačni proizvod) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)          | C11202<br>(trenutačni proizvod) |
| Planirana/tekuća klinička ispitivanja nakon stavljanja u promet                                                                 |                                 |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                      | C11202<br>(trenutačni proizvod) |
| Aktivnosti kliničkog praćenja nakon stavljanja u promet                                                                         |                                 |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(trenutačni proizvod) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(trenutačni proizvod) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(trenutačni proizvod) |

### 1.4.1 Sažetak podataka iz razdoblja prije stavljanja lijeka u promet (ispitivanja na životinjama i klinička ispitivanja)

U **tablici 1.4** u nastavku opisana su sva ispitivanja prije stavljanja u promet, i ona na životinjama i klinička.

**Tablica 1.4 Sažetci ispitivanja prije stavljanja u promet**

| Funkcionalna ispitivanja na životinjama prije stavljanja u promet |                                 |                             |                                                       |                                                           |                                                                                                |
|-------------------------------------------------------------------|---------------------------------|-----------------------------|-------------------------------------------------------|-----------------------------------------------------------|------------------------------------------------------------------------------------------------|
| Naziv ispitivanja                                                 | Godina / CI                     | Vrsta ispitivanja           | Ciljevi                                               | Ključne točke                                             | Kriteriji potencijalne prihvatljivosti                                                         |
| Biocompatibility and Biofunctionality of a Biodegradable Implant  | 2000.<br>Radi Medical System AB | Ispitivanje na životinjama; | Cilj ispitivanja bio je procijeniti biokompatibilnost | N = 3 odrasle ženke ovce, 1 životinja po vremenskoj točki | Prohodnost arterije<br>• Procjena protoka krvi nakon postavljanja – 2/3 smanjenje protoka krvi |

Sažetak o sigurnosnoj i kliničkoj učinkovitosti sustava FemoSeal™ VCS – korisnici / zdravstveni djelatnici



|                                                                                                                                                                                                        |                                         |                           |                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|---------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | Izvršilo društvo Biomatech iz Francuske | eksplorativno ispitivanje | i biofunktionalnost biorazgradivog implantata osmišljenog za postizanje hemostaze u vaskularnom sustavu. U izvješće su uključene rezervne životinje iz ispitivanja br. 862 (dokument br. 1051-01) | <p>Praćenje histopatoloških analiza, makroskopskih stupnjevanja i ultrastrukturne analize</p> <ul style="list-style-type: none"> <li>• 12 mjeseci</li> <li>• 15 mjeseci</li> <li>• 18 mjeseci</li> </ul> <p>Ultrazvučno praćenje color dopplerom – 30 dana na pristupnim mjestima na karotidnoj i femoralnoj arteriji</p> | <p>povezano s privremenim arterijskim vazospazmom koji se pripisivao zahvatu, do čega je došlo u lijevoj zajedničkoj karotidnoj arteriji</p> <ul style="list-style-type: none"> <li>• Ultrazvučna procjena color dopplerom (4 tjedna) – 3/3 (100 %) bez znatnog smanjenja protoka krvi 30 dana nakon implantacije</li> </ul> <p>Makroskopska zapažanja</p> <ul style="list-style-type: none"> <li>• 12 mjeseci – makroskopski potvrđena prohodnost na temelju izostanka anatomske vidljive okluzije; nisu se pojavile nikakve makroskopske lokalne netolerancije (krvarenje, nekroza ili neovaskularizacija); pokazalo se da je enkapsulacija unutarnjeg diska označena</li> <li>• 15 mjeseci – makroskopskim promatranjem nisu utvrđene nikakve upale; nisu identificirani nikakvi ostatci unutarnjeg ni vanjskog diska; inkapsulirano tkivo u području vanjskog diska pokazalo se istim kao i kod promatranja nakon 12 mjeseci</li> <li>• 18 mjeseci – makroskopskim praćenjem nisu utvrđeni nikakvi znakovi lokalne netolerancije, vanjski je disk bio vidljiv (3/3 slučaja), degradacija unutarnjeg diska potpuna; 1/3 (lijeva zajednička karotidna arterija) – depresija stijenke arterije uočena na mjestu implantacije (može biti povezana s postavljanjem proizvoda)</li> </ul> <p>Zaključci</p> <ul style="list-style-type: none"> <li>• Makroskopski, 12, 15 i 18 mjeseci nakon implantacije nisu otkriveni nikakvi</li> </ul> |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|---------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                                                                                                                                                                                                                                                                                |                                                                                    |                                                              |                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|--------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                                                                                                |                                                                                    |                                                              |                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                | <p>nekrotični, degenerativni ni trombotski znakovi.</p> <ul style="list-style-type: none"> <li>Pokazalo se da postupak razgradnje unutarnjih i vanjskih diskova traje između 12 i 18 mjeseci i djelovao je završen nakon 18 mjeseci, uz bjelkasto tkivo koje prekriva područje ugradnje.</li> <li>Histološki, nakon 18 mjeseci polimerni materijal više nije bio vidljiv, ali je bilo prisutno endoluminalno fibrozno tkivo. Nisu zabilježene nekrotične, degenerativne ni trombotske lezije.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                    |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002. Radi Medical System AB</p> <p>Izvršilo društvo Biomatech iz Francuske</p> | <p>Ispitivanje na životinjama; eksplorativno ispitivanje</p> | <p>Cilj ispitivanja bio je procijeniti biokompatibilnost biorazgradivog implantata s ciljem postizanja hemostaze u vaskularnom sustavu.</p> | <p>Praćenje (nakon implantacije)</p> <ul style="list-style-type: none"> <li>12 tjedana</li> <li>24 tjedna</li> <li>36 tjedana</li> </ul> <p>N = 12 ovaca, 3 životinje po vremenskoj točki, 3 rezervne životinje žrtvovane nakon 12, 15 i 18 mjeseci</p> <p>Mjesta implantacije – desna i lijeva femoralna arterija, desna i lijeva zajednička karotidna arterija</p> <p>Ultrazvučna analiza color doplerom</p> | <p>Prohodnost karotidnih i femoralnih arterija nakon 4 tjedna</p> <ul style="list-style-type: none"> <li>Velika redukcija protoka krvi 0/12 (0 %)</li> </ul> <p><u>Bez velikog smanjenja protoka krvi</u></p> <ul style="list-style-type: none"> <li>Teško oštećenje krvnog protoka povezano s uvođenjem proizvoda 0/12 (0 %)</li> <li>Smanjenje protoka krvi u lijevoj zajedničkoj karotidnoj arteriji 2/12 (16,6 %) zbog privremenog arterijskog vazospazma (za koji se smatralo da je povezan s kirurškim zahvatom, ne s proizvodom)</li> </ul> <p><u>Poremećaj protoka krvi prilikom praćenja</u></p> <p>12 tjedana – 0/12 (0 %)<br/>24 tjedna – 0/12 (0 %)<br/>36 tjedana – 0/12 (0 %)</p> <p>Mjerenja krvnog tlaka (3 ovce – 36 tjedana)</p> <ul style="list-style-type: none"> <li>Nije detektirano veliko smanjenje protoka krvi</li> </ul> <p>Makroskopski podatci za integraciju i razgradnju (stupanj 0 – 4)</p> |

|  |  |  |  |  | <u>Karotidne lokacije</u><br><u>Unutrašnja strana</u><br>- enkapsulacija<br>12 tjedana 1,3<br>24 tjedna 0,8<br>36 tjedana 0,7<br>- razgradnja materijala<br>12 tjedana 2,2<br>24 tjedna 2,3<br>36 tjedana 0,7<br><u>Vanjski dio</u><br>- enkapsulacija<br>12 tjedana 2,0<br>24 tjedna 1,0<br>36 tjedana 0,8<br>- razgradnja materijala<br>12 tjedana 2,0<br>24 tjedna 2,7<br>36 tjedana 3,2<br><br><u>Femoralne lokacije</u><br><u>Vanjski dio</u><br>- enkapsulacija<br>12 tjedana 1,0<br>24 tjedna 2,7<br>36 tjedana 1,0<br>- razgradnja materijala<br>12 tjedana 2,0<br>24 tjedna 2,4<br>36 tjedana 3,0<br><br><u>Unutrašnja strana</u><br>- enkapsulacija<br>12 tjedana 2,0<br>24 tjedna 1,2<br>36 tjedana 1,0<br>- razgradnja materijala<br>12 tjedana 1,0<br>24 tjedna 2,2<br>36 tjedana 3,0<br><br><u>Histološki podaci za integraciju, razgradnju i upalne parametre (srednja vrijednost relevantnih vrijednosti, indeks 0 – 4) n=6</u><br><br><u>Karotidne lokacije</u><br>Vanjska fibroza |
|--|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | 12 tjedana – 2,3<br>24 tjedna – 2,3<br>36 tjedana – 1,8<br>Unutarnja neointima<br>12 tjedana – 3,0<br>24 tjedna – 2,7<br>36 tjedana – 3,3<br>Smanjenje kvalitete materijala<br>12 tjedana – 1,7<br>24 tjedna – 3,0<br>36 tjedana – 3 +<br>Upalni parametri (makrofagi)<br>12 tjedana – 3,0<br>24 tjedna – 1,7<br>36 tjedana – 1,7<br><u>Femoralne lokacije</u><br>Vanjska fibroza<br>12 tjedana – 1,3<br>24 tjedna – 1,5<br>36 tjedana – 1,7<br>Unutarnja neointima<br>12 tjedana – 3,7<br>24 tjedna – 3,3<br>36 tjedana – 3,8<br>Smanjenje kvalitete materijala<br>12 tjedana – 2,0<br>24 tjedna – 3,0<br>36 tjedana – 3+<br>Upalni parametri (makrofagi)<br>12 tjedana – 3,5<br>24 tjedna – 1,8<br>36 tjedana – 1,8<br><br><u>Vrijednosti histomorfološke prohodnosti</u><br>Karotidne lokacije<br>12 tjedana 74,0 %<br>24 tjedna 81,9 %<br>36 tjedana 89,43 %<br>Femoralne lokacije<br>12 tjedana – 42,2 %<br>24 tjedna – 73,21 %<br>36 tjedana – 78,71 %<br><br><u>Prohodnost krvnih žila u SAD-u (srednja vrijednost %)</u><br>Karotidna lokacija<br>12 tjedana 94,6 % |
|--|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                                                                                                                                                                                                                                                                 |                                                                                    |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|----------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                                                                                 |                                                                                    |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                             | 24 tjedna – 96,7 %<br>36 tjedana – 94,7 %<br>Femoralne lokacije<br>12 tjedana – 66,9 %<br>24 tjedna – 63,6 %<br>36 tjedana – 75,1 %<br><br>Zaključci <ul style="list-style-type: none"> <li>Nije otkriven nikakav znak značajne lokalne netolerancije (odsutnost vidljivih upalnih, nekrotičnih i degenerativnih lezija) tijekom 12, 24 ili 36 tjedana</li> <li>Nema značajnih štetnih reakcija tkiva zabilježenih u vezi s domaćinom i proizvodom</li> <li>Razgradnja implantata gotovo je dovršena nakon 36 tjedana</li> </ul>                                                                               |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France). | 2002.<br><br>Radi Medical System AB<br><br>Izvršilo društvo Biomatech iz Francuske | Ispitivanje na životinjama | Svrha je ispitivanja bila procijeniti biokompatibilnost i biofunktionalnost biorazgradivog implantata osmišljenog za ° postizanje hemostaze u vaskularnom sustavu. Ispitani proizvod namijenjen je za ulazak u punkcijski otvor u arterijama radi postizanja hemostaze. Jedan disk ušao je u punkcijski otvor u arteriji, a drugi je zategnuo unutarnji disk izvan arterije. Oba diska umetnuta su kroz ovojnicu uvednice. Diskovi su osmišljeni za sprječavanje krvarenja, °zacjeljivanje u stijenku krvne žile te konačno razgradnju i apsorpciju. Ispitivanje je osmišljeno za prikupljanje i analizu podataka nakon funkcijske implantacije u ovaca | Razdoblje implantacije/praćenja je do 5 tjedana za sve životinje<br><br>4 ovce, 1 svinja<br><br>14 elemenata za zatvaranje<br><br>8 elemenata za zatvaranje ugrađenih u 2 ovce<br><br>2 elementa za zatvaranje ugrađena u 1 svinju<br><br>Kada su dva elementa za zatvaranje implantirana u istu femoralnu arteriju, implantirani su na udaljenosti > 30 mm | Svi kriteriji neželjenih znakova (upala, nekroza, krvarenje ili sve druge lezije) i svako stvaranje tankog pseudointimalnog sloja zabilježeni su. Posebna je pozornost posvećena početnoj tkivnoj integraciji proizvoda, s posebnim naglaskom na inkapsulaciju unutarnjeg diska.<br><br>Makroskopski, tamo gdje je promatrano, nisu uočeni nikakvi znakovi lokalne netolerancije ni stvaranja tromba. Makroskopskim promatranjem nisu utvrđene nikakve razlike između ovce i svinje nakon ugradnje elemenata za zatvaranje u femoralnim arterijama. Makroskopski, tamo gdje je promatrano, nisu uočeni nikakvi |

|  |  |  | <p>i svinja kako bi se ocijenio kapacitet implantata za održavanje fiziološke funkcije kada se upotrebljava u krvožilnom sustavu, u svrhu određivanja odgovora domaćina i odgovora proizvoda (fizička cjelovitost, tkivna enkapsulacija prilikom žrtvovanja) te kako bi se procijenila razgradnja implantata</p> |  | <p>znakovi lokalne netolerancije ni stvaranja tromba. Makroskopskim promatranjem nisu utvrđene nikakve razlike između ovce i svinje nakon ugradnje elemenata za zatvaranje u femoralnim arterijama.</p> <p>Histološkom analizom mjesta implantacije u ovaca nisu utvrđene nikakve lokalne nuspojave. Na unutarnjim i vanjskim diskovima utvrđeni su znakovi razgradnje i u nekim su slučajevima bili puknuli na manje dijelove. Unutarnji diskovi bili su potpuno integrirani u neointimalno tkivo. Histopatološka analiza u svinje pokazala je nešto više upalnih znakova oko unutarnjih i vanjskih diskova. Kod obje je životinje kod multifilamenta utvrđeno nešto više upalnih znakova nego kod materijala diska, što je normalno kod pletenoga kirurškog konca zbog većih površina.</p> <p>Prohodnost krvnih žila izmjerena je nakon 5 tjedana primjenom triju različitih metoda – histomorfometrijske, histomorfometrijske u kombinaciji s mjerenjem promjera žile s pomoću pomičnog mjerila i uporabom color dopplerskog ultrazvuka. Srednja prohodnost krvnih žila u ovce bila je između 60 i 80 %, ovisno o metodi</p> |
|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                                                                                                                                                                                                              |                               |                                                      |                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                 | (12 opažanja). U svinje srednja prohodnost krvnih žila bila je između 40 i 80 % (2 opažanja).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Prvo kliničko ispitivanje na ljudima</b>                                                                                                                                                                  |                               |                                                      |                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Naziv ispitivanja                                                                                                                                                                                            | Godina / CI                   | Vrsta ispitivanja                                    | Ciljevi                                                                                                                                                                                                                                                                                                                                  | Ključne točke                                                                                                                                                                                                                                                                                                                                                                                   | Kriteriji potencijalne prihvatljivosti                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004. Radi Medical Systems AB | Otvoreno multicentrično ispitivanje u jednoj skupini | Ciljevi ispitivanja bili su općenito utvrđivanje sigurnosti, učinka i učinkovitosti sustava FemoSeal Vascular Closure System (sustav FemoSeal) te posebno elemenata za zatvaranje u bolesnika koji se podvrgavaju dijagnostičkim ili intervencijskim kardiovaskularnim postupcima u kojima se upotrebljava pristup femoralnom arterijom. | 2-dijelno ispitivanje<br><br>Ukupno n = 80<br>1. dio n = 20<br>2. dio n = 60<br><br>Indikacije:<br>1. dio – dijagnostička kateterizacija srca uporabom femoralne arterije kao mjesta pristupa<br><br>2. dio – pacijenti koji se podvrgavaju dijagnostičkim i intervencijskim zahvatima na srcu kod kojih se femoralna arterija upotrebljava kao mjesto pristupa<br><br>Praćenje tijekom 30 dana | Ishodi<br><u>- hemostaza postignuta FS-om bez kompresije</u><br>- 1. dio 20/20 (100 %)<br>- 2. dio 58/60 (97 %)<br><br>Medijan vremena do hemostaze u vrijeme zahvata (2. dio) – 1,0 minuta (raspon odmah – 8 minuta)<br><br><u>Vrijeme do pokretljivosti (minute)</u><br>1. dio – medijan: 33,0<br>srednja vrijednost: 67,8<br>2. dio – medijan: 45<br>srednja vrijednost: 87,5<br><br><u>Incidencija glavnih vaskularnih komplikacija – praćenje tijekom 30 dana</u><br>1. dio<br>- bez vaskularnih komplikacija 20/20 (100 %)<br>2. dio<br>pseudoaneurizma – 1/59 (1,69 %)<br><br><u>Neuspješnost liječenja</u><br>1. dio – 0/20 (0%)<br>2. dio – 3/60 (5 %)<br>• 2 zbog neuspješnosti postizanja hemostaze |

|  |  |  |  |  | bez primjene kompresije<br>• 1 zbog velikih vaskularnih komplikacija, pseudoaneurizme<br><br><u>Dugotrajno curenje</u><br>1. dio – 0/20 (0%)<br>2. dio – 8/60 (13%)<br><br><u>Hematom</u><br>1. dio – 0/20 (0%)<br>2. dio – 6/60 (10%) |
|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Kao dio plana predtržišnog razvoja proizvoda FemoSeal™ VCS, provedena su 3 funkcionalna ispitivanja na životinjama. Godine 2000., prije početka kliničkih ispitivanja, provedeno je ispitivanje na životinjama za procjenu biofunkcionalnosti sustava FemoSeal™ VCS. Ovim je ispitivanjem procijenjena sposobnost elemenata za zatvaranje za održavanje fiziološke funkcije te je procijenjeno i njihovo razgrađivanje. Nakon 18 mjeseci, materijal unutarnjeg i vanjskog diska više nije bio vidljiv, zamijenjen je endoluminalnim fibroznim tkivom. Zaključno je potvrđen kapacitet elementa za zatvaranje sustava FemoSeal™ VCS za održavanje fiziološke funkcije kada se upotrebljava u cirkulacijskom sustavu.

Godine 2002. provedeno je ispitivanje na životinjama kako bi se ocijenila biokompatibilnost i biofunkcionalnost biorazgradivog implantata sustava FemoSea™ VCS, osmišljenog za postizanje hemostaze u vaskularnom sustavu. Ukratko, razgradnja implantata gotovo je dovršena za 36 tjedana i nije bilo nikakvih znatnih neželjenih tkivnih reakcija.

Još jednim ispitivanjem na životinjama 2002. godine procijenjene su biokompatibilnost i biofunkcionalnost biorazgradivog implantata sustava FemoSeal™ VCS, osmišljenog za postizanje hemostaze u vaskularnom sustavu. Nakon 5 tjedana, inkapsulacija diska bila je dovršena i bili su vidljivi znakovi razgradnje na unutarnjim i vanjskim diskovima. Zaključno, potvrđena je sposobnost implantata za održavanje fiziološke funkcije kada se upotrebljava u krvožilnom sustavu.

U sklopu plana kliničkog razvoja sustava FemoSeal™ VCS, društvo Radi Medical System AB provelo je kliničko ispitivanje prije stavljanja u promet. To kliničko ispitivanje nije objavljeno ni dostupno na internetu. Ispitivanje s modelom proizvoda br. 11200 provedeno je 2002. – 2004. U skladu s europskom normom EN 540 (Kliničko ispitivanje medicinskih proizvoda za ljude)



i u skladu s općim smjernicama ICH-a za klinička ispitivanja i smjernicama za dobru kliničku praksu. Pojediniosti o ovom ispitivanju dokumentirane su u izvještaju EU-SE-001. To kliničko ispitivanje dokumentirano je u završnom izvještaju društva Radi Medical Systems AB, „Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures”. Kliničko ispitivanje provedeno je s prvim modelom sustava FemoSeal™ br. 11200 te je bilo usredotočeno na sigurnost i učinkovitost ugrađivih komponenti za zatvaranje. Jedina razlika između prvog modela br. 11200 i aktualnog modela C11202 je veličina u frenchima, 6 F i 7 F, te poboljšani sustav uvođenja. Kliničke koristi, namjena, načela rada i sirovine ugrađivih elemenata za zatvaranje, unutarnja brtva i vanjski disk za zaključavanje ostaju nepromijenjeni.

Proizvod je bio namijenjen za pacijente podvrgnute dijagnostičkim ili intervencijskim kardiološkim zahvatima u kojima se kao pristupna točka upotrebljava femoralna arterija. Cilj tog ispitivanja bio je utvrditi sigurnost, učinak i učinkovitost sustava FemoSeal™ VCS. Bilo je to prospektivno, multicentrično, otvoreno ispitivanje jedne skupine s 30-dnevnim praćenjem.

Primarna mjera ishoda učinkovitosti bilo je vrijeme do hemostaze definirane kao odsutnost snažnog krvarenja. Primarna sigurnosna mjera ishoda bila je pojava velikih vaskularnih komplikacija tijekom 30 dana. Sekundarne mjere ishoda obuhvaćale su vrijeme do pokretljivosti, udio neuspješnog liječenja, incidencija štetnih događaja i značajke funkcije proizvoda tijekom uvođenja i postavljanja.

Pacijenti uključeni u to ispitivanje bili su odrasli koji su mogli dati informirani pristanak te imali neoštećen puls na najmanje jednom stopalu. Pacijenti su bili isključeni iz ispitivanja ako su imali bilo koje od sljedećih stanja:

- povijest bolesti perifernih krvnih žila
- autoimune bolesti
- poznati poremećaj krvarenja ili tešku anemiju
- INR >1,5
- infarkt miokarda unutar 72 sata
- nekontrolirana hipertenzija unatoč liječenju
- pretilost koja sprečava pristup Seldingerovom tehnikom
- prisutnost vaskularnog presatka ili stenta na mjestu arteriotomije
- prethodna ipsilateralna punkcija unutar 3 mjeseca
- očekivano trajanje života < 6 mjeseci.

Osim toga, pacijenti su intraoperativno pregledani i isključeni iz ispitivanja ako je zapaženo bilo što od sljedećeg:

- promjer lumena zajedničke femoralne arterije <5 mm
- arterijske grane unutar 2 cm proksimalno od mjesta punkcije
- značajna stenoza unutar 3 cm od mjesta punkcije
- uporaba primarne uvodnice ovojnice > 6 Fr
- punkcija na mjestu bifurkacije femoralne arterije ili distalno od nje
- višestruke femoralne punkcije
- poznate ili suspektne punkcijske ozljede stražnje stijenke femoralne arterije
- veliki hematoma (2:6 cm) nakon dovršetka zahvata
- teško uvođenje primarne ovojnice za zahvat zbog tortuoznog tkiva ili krvne žile.

To ispitivanje prema jednom planu ispitivanja provedeno je u dva dijela: tijekom 1. dijela uključeno je 20 pacijenata, zatim je izrađena sigurnosna analiza, a potom je u 2. dijelu uključeno dodatnih 60 pacijenata.

U 1. dijelu srednja dob uključenih pacijenata bila je 65,9 godina, 70,0 % bolesnika bili su muškarci, a 95 % bolesnika uzimalo je druge lijekove. U 2. dijelu ispitivanja srednja dob bila je 63,8 godina, 78 % bili su muškarci, a 100 % ispitanika uzimalo je druge lijekove.

Za uključivanje u ispitivanje prihvatljivi su bili pacijenti koji se podvrgavaju dijagnostičkim (1. i 2. dio) ili intervencijskim (2. dio) zahvatima kateterizacije srca. Zahvati su bili u skladu sa standardom njege u svakoj od bolnica u kojima su se uključivali pacijenti, nakon čega je slijedila primjena sustava FemoSeal™ VCS. Podatci o pacijentima prikupljeni su na početku ispitivanja, tijekom zahvata te 1 dan i 30 dana nakon zahvata. Rezultati su sažeti u **tablici 1.5** i pokazuju da je sustav FemoSeal™ VCS siguran i učinkovit za uporabu u toj populaciji pacijenata.

**Tablica 1.5 Klinički rezultati navedeni u ispitivanju prije stavljanja u promet**

|                                                           | 1. dio      | 2. dio                   |
|-----------------------------------------------------------|-------------|--------------------------|
| Broj pacijenata                                           | 20          | 60                       |
| Prosječno vrijeme do hemostaze                            | 1,2 minute  | 1,6 minuta <sup>a</sup>  |
| Srednje vrijeme do pokretljivosti                         | 72,2 minute | 87,5 minuta <sup>b</sup> |
| Incidencija glavnih vaskularnih komplikacija <sup>c</sup> | 0 (0 %)     | 1 (2 %)                  |

|                                                                                                                 |          |           |
|-----------------------------------------------------------------------------------------------------------------|----------|-----------|
| Broj pacijenata sa štetnim događajima                                                                           | 5 (25 %) | 19 (32 %) |
| Neuspješnost liječenja (definirana kao velike vaskularne komplikacije, potreba za ručnom kompresijom ili oboje) | 0 (0 %)  | 3 (5 %)   |
| Kvarovi proizvoda                                                                                               | 0 (0 %)  | 6 (10 %)  |

<sup>a</sup> Na temelju ukupne veličine uzorka od 58 pacijenata jer u 2 pacijenta nije postignuta hemostaza u vrijeme zahvata zbog prethodnih ipsilateralnih punkcija. Hemostaza je u tih pacijenata ostvarena nakon 7 minuta i 37 minuta.

<sup>b</sup> Na temelju ukupne veličine uzorka od 59 pacijenata: 1 pacijent nije bio uključen jer je bio postavljen na respirator zbog plućnog edema te dulje od tjedan dana nije bio pokretan.

<sup>c</sup> Definirane kao vaskularne komplikacije koje zahtijevaju transfuziju krvi ili kirurški popravak, lokalna infekcija koja zahtijeva primjenu antibiotika, hospitalizaciju ili produljenje hospitalizacije ili ekscizija rane na mjestu zahvata.

U 1. dijelu ispitivanja nisu zapažene nikakve ozbiljne vaskularne komplikacije. U 2. dijelu ispitivanja prijavljena je jedna velika vaskularna komplikacija: pseudoaneurizma koja je zabilježena u roku od jednog dana nakon zahvata. Kod tog događaja bila je potrebna kompresija pod ultrazvučnim vođenjem i injekcija trombina u pseudoaneurizmu te produljenje pacijentove hospitalizacije.

Od pet štetnih događaja prijavljenih u 1. dijelu ispitivanja, došlo je do jednog štetnog događaja potencijalno povezanog s proizvodom: štetni događaj, koji nije bio ozbiljan, snažnog krvarenja 1 dan nakon zahvata. Od 19 štetnih događaja prijavljenih u 2. dijelu ispitivanja uočena su tri štetna događaja hematoma povezana s proizvodom, a koji nisu bili ozbiljni, kao i šest štetnih događaja moguće povezanih s proizvodom koji nisu bili ozbiljni, a obuhvaćali su tri izvještaja o dugotrajnom curenju, dva hematoma i jednu bol u nozi nakon tjelovježbe.

U 2. dijelu 3 pacijenta smatrala su se neuspješnima u liječenju: 2 zbog nemogućnosti postizanja hemostaze bez primjene kompresije i 1 zbog velike vaskularne komplikacije (pseudoaneurizme). Nije bilo neuspješnog liječenja u 1. dijelu ispitivanja.

Od šest kvarova proizvoda u 2. dijelu ispitivanja tri nisu ometala zahvat, jedan je bio pripisan korisničkoj grešci, jedan se odnosio na curenje iz uvodnice, a jedan je bio puknuće zgloba filamenta. Posljednja su dva problema obuhvaćena implementiranjem ažuriranja modela u C11202.

U 2. dijelu kliničkog ispitivanja prije stavljanja u promet nisu bili prijavljeni rezultati 6-mjesečnog praćenja zbog pacijentova nepridržavanja plana ispitivanja. Rezultati nakon kliničkog

ispitivanja prije stavljanja u promet (EU-SE-001) nakon 30 dana, što je u skladu s razdobljem praćenja iz kliničke literature, pokazuju da je sustav FemoSeal™ VCS siguran i učinkovit.

### 1.4.2 Sažetak podataka iz kliničkih ispitivanja nakon stavljanja u promet

U **tablici 1.6** u nastavku opisana su četiri klinička ispitivanja nakon stavljanja u promet. Ta klinička ispitivanja nisu objavljena ni dostupna na internetu.

**Tablica 1.6 Kliničke studije nakon stavljanja lijeka u promet**

| Završena klinička ispitivanja nakon stavljanja u promet                                     |                                                          |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|---------------------------------------------------------------------------------------------|----------------------------------------------------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------|----|-----|----------|-------|----------|-----------|----|-----------|-----------|-------------------------|----------|--------------------|------------|---------------------|-----------|-------------------|---------|-----------------------|----------|--------------------------------|----------|----------------------|-----------|--------------------------|-----------|-----------------------------------|----------|----------------------|--------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Naziv ispitivanja                                                                           | Godina / CI                                              | Vrsta ispitivanja                                                                 | Ciljevi                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Ključne točke                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Kriteriji potencijalne prihvatljivosti                                                                                                    |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006. RADI                                               | Ispitivanje nakon stavljanja u promet, prihvatljivo st nove ambalaže za korisnike | Ispitivanje nakon stavljanja u promet provedeno na ažuriranom modelu FemoSeal Vascular® Closure System br. 11202, koji ima modificirani sustav uvođenja u usporedbi s prvim modelom, br. 11200, za dokumentiranje funkcionalnosti.<br><br>Cilj ispitivanja bio je dobiti povratne informacije o revidiranim uputama za uporabu, projektu obuke za liječnike i medicinske sestre, potvrditi procjene analize rizika te kako bi se dobile informacije o svim poboljšanjima kvalitete proizvoda. | 100 pacijenata <ul style="list-style-type: none"><li>63 muškarca / 37 žena</li><li>Srednja dob 68 godina za žene, 65 godina za muškarce</li></ul> 2 švedske bolnice, 6 liječnika<br><br>112 proizvoda<br><br>Podatci prikupljeni u test-listama pacijenata (engl. Case Report Form, CRF)<br><br>Planirano vrijeme promatranja – 30 minuta od vremena primjene                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Ishodi<br><br>1. Ilustracije/upute u uputama za uporabu smatraju se informativnima i primjerenima<br><br>2. Trenutačna hemostaza (91/100) |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)           | Dr. Nicolas Moes, Innsbruck Medical University, Austrija | Potvrдна procjena nakon stavljanja u promet                                       | Cilj ovog ispitivanja bio je procijeniti sigurnost i učinkovitost sustava FemoSeal® korištenog tijekom uobičajene kliničke rutine u bolesnika podvrgnutih dijagnostičkoj kateterizaciji srca ili perkutanom intervencijskom zahvatu na srcu obavljenom s pomoću uvodne ovojnice od 7 F.                                                                                                                                                                                                       | 50 uzastopnih pacijenata<br><br>Indikacija – dijagnostička ili invazivna kateterizacija srca iz zajedničke femoralne arterije<br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                         | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Primarne mjere ishoda <ul style="list-style-type: none"><li>Primarna mjera ishoda učinkovitosti – vrijeme do hemostaze s curenjem ili bez njega, ali bez dodatne kompresije, ručne ili mehaničke.</li><li>Sigurnosna mjera ishoda – incidencija štetnih događaja – manje i veće vaskularne komplikacije i svi ostali štetni događaji – ozbiljni i oni koji nisu ozbiljni tijekom trajanja ispitivanja (tj. do otpuštanja pacijenta).</li></ul> Ishodi |
| n                                                                                           | 50                                                       |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| men                                                                                         | 35 (70%)                                                 |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| women                                                                                       | 15 (30%)                                                 |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| PCI cases                                                                                   | 15                                                       |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| age (yrs)                                                                                   | 62.8±11.1                                                |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| body mass index (kg/m²)                                                                     | 25.4±6.7                                                 |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| systolic BP (mmHg)                                                                          | 131.2±20.9                                               |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| diastolic BP (mmHg)                                                                         | 77.9±10.6                                                |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| diabetes mellitus                                                                           | 9 (18%)                                                  |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| arterial hypertension                                                                       | 34 (68%)                                                 |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| previous coronary intervention                                                              | 13 (26%)                                                 |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| preprocedure aspirin                                                                        | 50 (100%)                                                |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| preprocedure clopidogrel                                                                    | 50 (100%)                                                |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Procedural unfractionated heparin                                                           | 15 (30%)                                                 |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Procedural abciximab                                                                        | 2 (4%)                                                   |                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |

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|--------------------------------------------------------------------------------|---------------------------------|---------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                |                                 |                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                 | <ul style="list-style-type: none"> <li>Prosječno vrijeme do hemostaze</li> <li>Dijagnostika – <math>56,6 \pm 29</math> sekundi</li> <li>Intervencija <math>59,9 \pm 16,2</math> sekunde</li> <li>Svi pacijenti <math>57,8 \pm 26,3</math></li> <li>Svi pacijenti bili su pokretni nakon 4 sata mirovanja u krevetu bez ikakvih problema.</li> </ul> <p>Sigurnosni ishodi</p> <ul style="list-style-type: none"> <li>49/50 (98 %) bez vaskularnih komplikacija do otpuštanja iz bolnice</li> <li>Prosječno vrijeme do otpuštanja 2,6 dana</li> <li>1/50 (2 %) slučaj manjeg krvarenja sljedećeg dana nakon što je pacijent na dan angiografije bio pokretan bez ikakvih poteškoća</li> </ul> |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009) | 2009. RADI                      | Ispitivanje nakon stavljanja u promet | <p>Ispitivanjem treba utvrditi jesu li kupci/korisnici uočili bilo kakve probleme s novom ambalažom, osobito s nesterilnom vanjskom stranom vrećice Tuvek/PET-PE.</p> <p>Ispitivanje također treba pružiti informacije o tome prepoznaje li liječnik bilo kakve razlike u fazama primjene/postavljanja proizvoda u usporedbi s prethodno korištenim proizvodima.</p> <p>Ispitivanjem je potrebno dobiti i povratne informacije o svim daljnjim potrebama za poboljšanje kvalitete proizvoda.</p> | <p>25 proizvoda</p> <p>4 švedske bolnice</p> <p>16/25 (64 %) bolesnika bili su bolesnici podvrgnuti perkutanoj koronarnoj intervenciji na jakoj antikoagulacijskoj terapiji</p> | <p>Ishodi</p> <ol style="list-style-type: none"> <li>Problemi povezani s pakiranjem – 21/25 (84 %) primjene bile su uspješne; 4/25 (16 %) su bile neuspješne (1 – ispitivanje nove uvednice, 1 unutarnji disk prošao je kroz arteriotomiju na koraku povlačenja, gumb je iskočio i vanjski je disk postavljen u kanal zarezanog tkiva, 2 trenutačna hemostaza nije postignuta unatoč tome što nije bilo problema prilikom postavljanja).</li> <li>Trenutačna hemostaza 19/25 (76 %) pacijenata</li> <li>Krvarenje 11/25 (44 %) – 9/25 (36 %) curenje/krvarenje, 2/25 (8 %) hematoma</li> </ol> <p>Ukupna stopa događanja 19 %</p>                                                           |
| The FemoSeal Vascular Closure System (VCS)                                     | 2022/Terumo Medical Corporation | Prospektivno, multicentrično          | Cilj je ovog ispitivanja dodatno dokazati sigurnost i učinkovitost sustava                                                                                                                                                                                                                                                                                                                                                                                                                       | <ul style="list-style-type: none"> <li>Praćenje pacijenta nakon 30 dana (<math>\pm 7</math> dana) posjetom bolnici ili telefonskim pozivom.</li> </ul>                          | <ul style="list-style-type: none"> <li><b>Demografija/komorbiditeti:</b></li> <li>- Spol: 161 muškarac (70 %) / 69 žena (30 %).</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |

|                                                                                                      |                                                                            |                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Registry: A<br>Prospective, Multi-<br>Center, Observational<br>Study in<br>Europe (T138E4)<br>(2022) | no,<br>opservacijs<br>ko<br>ispitivanje<br>nakon<br>stavljanja<br>u promet | FemoSeal™ VCS pri<br>postizanju hemostaze<br>pristupnih mjesta na<br>zajedničkoj femoralnoj<br>arteriji na stvarnim<br>pacijentima podvrgnutima<br>perkutanim endovaskularnim<br>zahvatima | <ul style="list-style-type: none"> <li>• Uključivanje pacijenata: od prosinca 2021. do srpnja 2022.</li> <li>• 230 uključenih ispitanika koji se podvrgavaju dijagnostičkim ili intervencijskim endovaskularnim zahvatima u kojima se upotrebljava FemoSeal™.</li> </ul> <p>3 europska mjesta ispitivanja:<br/>Francuska (92 pacijenta),<br/>Njemačka (38 pacijenata),<br/>Belgija (100 pacijenata).</p> | <ul style="list-style-type: none"> <li>- Srednja dob: 70 ± 12.</li> <li>- BMI: 26,1 ± 4,95 kg/m2.</li> <li>- Hipertenzija: 160 pacijenata (69,6 %).</li> <li>- Dislipidemija: 128 (55,7 %).</li> <li>- Bolest koronarnih arterija: 42 (18,3 %).</li> <li>- Trenutačni pušač: 86 (37,6 %).</li> <li>- Bivši pušač: 66 (28,8 %).</li> <li>- Koronarna bolest srca: 34 (14 %).</li> <li>- Prethodni infarkt miokarda: 18 (7,8 %).</li> <li>- Revaskularizacija perifernih arterija: 12 (5,2 %) karotidne arterije i 83 (37,5 %) arterije donjih ekstremiteta.</li> <li>- Antitrombocitna terapija (na početku ispitivanja): 211 (91,7 %), uključujući 21 (9,1 %) dvostruku antitrombocitnu terapiju (DAPT).</li> <li>- Oralna antikoagulacija: 40 (17,4 %) pacijenata.</li> <li>• <b>Karakteristike intervencije:</b> <ul style="list-style-type: none"> <li>- Postavka: 162 bolnička slučaja (70,4 %), 68 ambulantnih slučajeva (29,6 %).</li> <li>- Prevladavajuća indikacija: klaudikacija 147 slučajeva (63,9 %).</li> <li>- Način postupanja: 35 antegradnih (15,3 %), 194 retrogradna (84,7 %).</li> </ul> </li> <li>• <b>Primarne mjere ishoda:</b> <ul style="list-style-type: none"> <li>- Kombinirana mjera ishoda sigurnosti (bez većih komplikacija na mjestu pristupa u roku od 6 sati nakon zahvata) i učinkovitosti (uspješna hemostaza na mjestu punkcije) postignuta u 215/226 (95,1 %) [95 % CI: 91,46; 97,55]</li> </ul> </li> </ul> |
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|  |  |  |  |  | <p>pacijenata iz skupa za potpunu analizu te 215/230 (93,5 %) [95 % CI 89,47, 96,30] u skupu pacijenata liječenih proizvodom FemoSeal™.</p> <p>- Mjera ishoda postignuta je u 219/226 (96,9 %) pacijenata (CI 93,7, 98,7).</p> <p>- Sigurnosna mjera ishoda postignuta u 220/230 (95,2 %) [95 % CI: 92,15, 97,90] pacijenata.</p> <p>• <b>Sekundarne mjere ishoda:</b></p> <p>- Izostanak manjih komplikacija na mjestu pristupa šest sati nakon zahvata postignuta je u 225/230 (97,8 %) [95 % CI: 95,00; 99,29].</p> <p>- Izostanak velikih i manjih komplikacija na mjestu pristupa od šest sati do 30 dana nakon zahvata postignut je u 219/230 (95,2%) pacijenata [95% CI: 91,60; 97,59].</p> <p>- Medijan vremena do hemostaze s FemoSeal™ VCD-om: 0,42 (0,25; 0,50) minuta.</p> <p>- Medijan vremena do pokretljivosti: 5,00 (4,54; 5,50) minuta.</p> <p>- Medijan boravka u bolnici: 23,98 (22,72, 25,00) sati.</p> <p>- Upotrebljivost FemoSeal™ VCS-a: „jednostavno“ ili „vrlo jednostavno“ za postavljanje u 98,7% slučajeva („jednostavno“ za postavljanje u 21 (9,2%), „vrlo jednostavno“ za postavljanje u 205 (89,5%)) bez ili s niskim</p> |
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|  |  |  |  |  | otporom pri postavljanju<br>u 226 (98,3%) slučajeva.<br>152/230 (66,1%) pacijenata<br>liječenih žicom vodicom<br>uključenom u komplet<br>FemoSeal™ (GW 0,038")<br>i preporučenom za<br>FemoSeal™ bez prijavljenih<br>nedostataka proizvoda ili<br>štetnih događaja. |
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Ispitivanje iz 2006. provedeno je kako bi se potvrdila sigurnost i učinkovitost trenutnog uređaja s poboljšanim sustavom uvođenja te kako bi se dobile povratne informacije o uputama za uporabu i programu obuke za sustav FemoSeal™ VCS. Ispitivanje je obuhvaćalo 100 pacijenata i primarna mjera ishoda bila je li postignuta hemostaza ili je bila potrebna dodatna ručna ili mehanička kompresija. Ovim je ispitivanjem zaključeno da je primjena sustava FemoSeal™ VCS u većini slučajeva bila uspješna (u 91 % postignuta je trenutna hemostaza).

U ispitivanje iz 2008. uključeno je 50 pacijenata radi procjene sigurnosti i učinkovitosti sustava FemoSeal™ VCS pri uporabi u normalnim kliničkim postupcima u pacijenata podvrgnutih kateterizaciji srca s pomoću uvodnice od 7 Fr. Primarna mjera ishoda ispitivanja bilo je prikupljanje podataka o vremenu do hemostaze i vremenu do pokretljivosti bez dodatne kompresije, ručne ili mehaničke. Prema rezultatima ispitivanja zaključeno je da je srednje vrijeme do hemostaze iznosilo 57,8 sekundi te da su svi pacijenti bili pokretni nakon 4 sata ležanja u krevetu.

Ispitivanjem iz 2009. procjenjivalo se novo pakiranje sustava FemoSeal™ VCS. U ispitivanje je bilo uključeno dvadeset i pet pacijenata. Primarna mjera ishoda bila je je li korisnik imao bilo kakvih problema s ambalažom. Korisnici nisu primijetili nikakve probleme u vezi s novom ambalažom sustava FemoSeal™ VCS. Ovim ispitivanjem prikupljali su se i podaci o vremenu do postizanja hemostaze.

Cilj je tog ispitivanja iz 2022. bio proaktivno prikupiti podatke o sigurnosti i učinkovitosti sustava FemoSeal VCS pri postizanju hemostaze pristupnih mjesta na zajedničkoj femoralnoj arteriji na stvarnim pacijentima podvrgnutima perkutanom endovaskularnim zahvatima. U ispitivanje je bilo uključeno 230 pacijenata. Primarne mjere ishoda tog registra su uspješnost zahvata (tj. uspješnost hemostaze na mjestu punkcije) i smanjenje glavnih komplikacija (npr. ozljeda vaskularnog sustava, krvarenje povezano s pristupnim mjestom, infekcija na mjestu pristupa, ponovna ručna kompresija i nova ipsilateralna akutna ishemija noge povezana s pristupom). Studija je zaključila da FemoSeal™ VCS dobro funkcionira u stvarnim uvjetima te osigurava učinkovitu hemostazu i nisku stopu komplikacija na mjestu pristupa za pacijente koji se podvrgavaju perifernim endovaskularnim intervencijama. Pokazuje dobre performanse s



kratkim vremenom do hemostaze i dobrom povratnom informacijom o upotrebljivosti za operatera, što FemoSeal™ VCS čini vrijednim uređajem za zatvaranje femoralnog pristupa.

### 1.4.3 Sažetak podataka iz kliničkog praćenja nakon stavljanja lijeka u promet

#### 1.4.3.1 Završeno kliničko praćenje nakon stavljanja u promet

Sažetak dovršenih aktivnosti kliničkog praćenja nakon stavljanja na tržište opisan je u **Tablici 1.7** u nastavku.

**Tablica 1.7. Aktivnosti kliničkog praćenja nakon stavljanja lijeka na tržište**

| Završene aktivnosti kliničkog praćenja nakon stavljanja lijeka u promet   |             |                                                                               |                                                                                                                                                                                                       |                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|---------------------------------------------------------------------------|-------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Naziv aktivnosti                                                          | Godina / CI | Vrsta ispitivanja                                                             | Ciljevi                                                                                                                                                                                               | Ključne točke                                                                                                                                                                                                          | Kriteriji potencijalne prihvatljivosti                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021 TMC    | Kliničko ispitivanje nakon stavljanja u promet - visokokvalitetno ispitivanje | Anketa nakon stavljanja na tržište za prikupljanje potencijalnih povratnih informacija u vezi s upotrebom uređaja za vaskularno zatvaranje FemoSeal™ koji se distribuira na tržištima Europske unije. | <ul style="list-style-type: none"> <li>120 slučajeva</li> <li>8 različitih liječnika s &gt; 5 godina iskustva</li> <li>Više zemalja u Europi</li> </ul>                                                                | <b>1-5 Procjene uređaja na ljestvici – Anketne izjave</b> <ul style="list-style-type: none"> <li>Kriterij prihvatljivosti               <ul style="list-style-type: none"> <li>Ocjene 3 – 5 smatraju se povoljnima</li> <li>Sve izjave trebaju imati ≥ 80% pozitivnih povratnih informacija</li> </ul> </li> <li>Ishodi               <ul style="list-style-type: none"> <li>Nijedna izjava u ispitivanju nije primila &gt; 20% nepovoljnih odgovora</li> <li>Nije uložena nijedna pritužba na proizvod</li> </ul> </li> </ul> |
| 20210298 – 0.035” and 0038” Guidewire Clinical Survey Report (2021)       | 2021 TMC    | Kliničko ispitivanje nakon stavljanja u promet - visokokvalitetno ispitivanje | Ispitivanje nakon stavljanja na tržište radi prikupljanja prospektivnih povratnih                                                                                                                     | <ul style="list-style-type: none"> <li>Ispitivanja za žicu od 0,035               <ul style="list-style-type: none"> <li>106 anketa</li> <li>64 liječnika</li> </ul> </li> <li>Ispitivanja za žicu od 0,038</li> </ul> | <b>1-5 Procjene uređaja na ljestvici – Anketne izjave</b> <ul style="list-style-type: none"> <li>Kriterij prihvatljivosti               <ul style="list-style-type: none"> <li>Ocjene 3 – 5 smatraju se povoljnima</li> </ul> </li> </ul>                                                                                                                                                                                                                                                                                      |

| Završene aktivnosti kliničkog praćenja nakon stavljanja lijeka u promet                                                         |                     |                                                                               |                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                          |
|---------------------------------------------------------------------------------------------------------------------------------|---------------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                 |                     |                                                                               | <p>informacija povezanih s upotrebom žice vodilice od 0,035" uključene u proizvod Angio-Seal™ VIP Vascular Closure Device (VCD) od 6 Fr i žice vodilice od 0,038" uključene u proizvod Angio-Seal™ VIP VCD od 8 Fr i sustav FemoSeal Vascular Closure System distribuirane na tržištima Europske unije.</p> | <ul style="list-style-type: none"> <li>○ 109 anketa</li> <li>○ 55 liječnika</li> <li>• 12 retrospektivnih anketa</li> </ul>                                                                                                                                                                                                               | <ul style="list-style-type: none"> <li>○ Sve izjave trebaju imati <math>\geq 80\%</math> pozitivnih povratnih informacija</li> <li>• Ishodi <ul style="list-style-type: none"> <li>○ Sve su žice vodilice dobile prihvatljive ocjene</li> <li>○ Nije uložena nijedna pritužba na proizvod</li> </ul> </li> </ul>                                                                                         |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024<br>TMC/TE | Kliničko ispitivanje nakon stavljanja u promet - visokokvalitetno ispitivanje | <p>Prospektivno prikupljanje povratnih informacija povezanih s upotrebom sustava FemoSeal VCS sa žicama vodilicama koje se distribuiraju na tržištu EU-a.</p>                                                                                                                                               | <ul style="list-style-type: none"> <li>• 126 anketa</li> <li>• 7 lokacija</li> <li>• 5 zemalja</li> <li>• 14. studenog 2023. - 11. lipnja 2024.</li> <li>• Liječnik medicinske specijalnosti: <ul style="list-style-type: none"> <li>○ Vaskularni kirurg</li> <li>○ Intervencijski radiolog</li> <li>○ Angiologija</li> </ul> </li> </ul> | <p>Procjena proizvoda prema ljestvici 1–5 – izjave u istraživanju</p> <ul style="list-style-type: none"> <li>• Kriterij prihvatljivosti <ul style="list-style-type: none"> <li>○ Ocjene 3 – 5 smatraju se povoljnima</li> <li>○ Sve izjave trebaju imati <math>\geq 80\%</math> pozitivnih povratnih informacija</li> <li>○ Ako se u ovom ispitivanju pojave štetni događaji, oni</li> </ul> </li> </ul> |

| Završene aktivnosti kliničkog praćenja nakon stavljanja lijeka u promet |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-------------------------------------------------------------------------|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                         |  |  |  |  | <p>bi trebali biti oni koje je predvidjelo upravljanje rizikom.</p> <ul style="list-style-type: none"> <li>• Demografija pacijenata               <ul style="list-style-type: none"> <li>○ Žensko: 29,4% (37/126)</li> <li>○ Muško: 69,8% (88/126)</li> <li>○ Spol nije naveden: 0,8 (1/126)</li> <li>○ Dob &gt; 75 godina: 31,7%</li> </ul> </li> <li>• Ishodi               <ul style="list-style-type: none"> <li>○ Žica vodilica isporučena s proizvodom FemoSeal™ VCS: 101/126 (80,2%).</li> <li>○ Trajanje postupka (u minutama): 63,4 (36,6) (srednja vrijednost (SD)); 57,0 (36,0-81,0) (srednja vrijednost (IQR))</li> <li>○ Sve ocjene učinkovitosti sustava FemoSeal™ VCS bile su povoljne.</li> <li>○ Sve ocjene žice vodilice</li> </ul> </li> </ul> |

| Završene aktivnosti kliničkog praćenja nakon stavljanja lijeka u promet |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                          |
|-------------------------------------------------------------------------|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                         |  |  |  |  | <p>isporučene sa sustavom FemoSeal™ VCS bile su povoljne.</p> <ul style="list-style-type: none"> <li>○ Jedan štetni događaj (0,8 %): diskovi sustava FemoSeal™ VCS nisu bili dobro poravnati vjerojatno zbog upotrebe krute žice vodilice (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 inča) koja zahtijeva ručnu kompresiju za postizanje hemostaze.</li> </ul> |

Tvrtka Terumo Medical Corporation ispunila je tri visokokvalitetna upitnika za liječnike tijekom trenutnog izvještajnog razdoblja (01. rujna 2019. - 31. kolovoza 2024.).

Kliničkim anketama o proizvodu FemoSeal™ prikupljeni su proaktivni klinički podaci o sigurnosti i učinkovitosti sustava FemoSeal™ VCS tijekom kliničke uporabe. Anketa je obuhvaćala pitanja usmjerena na cijeli proizvod i povezani pribor, uključujući žicu vodilicu od 0,038", te njihove međusobne interakcije. Kliničkim anketama o žici vodilici prikupljeni su proaktivni klinički podatci o sigurnosti i učinkovitosti tijekom kliničke uporabe žice vodilice od 0,038" isporučene uz sustav FemoSeal™ VCS. Anketna pitanja bila su posebno usmjerena na opću uporabu žice vodilice u rasponu od uvođenja kroz ovojnicu u krvnu žilu do vađenja žice.

Sustav FemoSeal™ VCS i žica vodilica od 0,038" uključena uz proizvod dobili su sve prihvatljive ocjene, a podneseno je šest (6) pritužbi za proizvod te devet (9) napomena koje nisu

bile pritužbe u vezi sa žicom vodilicom na temelju procjene komentara dobivenih iz tih visokokvalitetnih kliničkih ispitivanja. Pritužbe su procijenjene i za FemoSeal i za žicu vodilicu, a procijenjene su u okviru postupka praćenja nakon stavljanja u promet društva Terumo. Nisu utvrđeni nikakvi novi rizici ni razine rizika.

Anketa liječnika-korisnika dovršena je 2024. kao dio aktivnosti PMCF-a. Rezultati ankete pokazali su da su ocjena učinkovitosti i sigurnost sustava FemoSeal™ VCS sveukupno vrlo povoljni. Dokazana je i kompatibilnost žica vodilica koje nisu standardne i koje se isporučuju sa sustavom FemoSeal™ VCS.

#### **1.4.3.2 Stalno/planirano kliničko praćenje nakon stavljanja u promet**

TMC ima jednu trenutačnu/planiranu aktivnost kliničkog praćenja nakon stavljanja u promet. Izvršit će se klinička anketa radi prospektivnog prikupljanja povratnih informacija u vezi s uporabom žice vodilice sa sustavom FemoSeal VCS distribuiranim na tržištu EU-a. Liječnici će ispuniti anketu kako bi se proučilo koje su žice vodilice upotrebljavali tijekom zahvata. Svrha ove ankete je riješiti nedostatak identificiran kao nedostatak literature i komentara vanjskih recenzenata o kompatibilnosti sustava FemoSeal™ VCS s upotrebom drugih žica vodilica koje nisu marke Terumo. Povratne informacije uključuju tehničke ishode, kliničku učinkovitost i sigurnost koji se odnose na učinkovitost proizvoda s različitim žicama vodilicama.

#### **1.4.4 Sažetak podataka iz sustavnog pregleda literature**

Terumo Medical Corporation provodi sustavne preglede literature radi prikupljanja i procjene kliničkih podataka o sigurnosti i učinkovitosti iz objavljenih ispitivanja proizvoda FemoSeal™ VCS i/ili sličnih proizvoda. Cilj je godišnjeg pregleda objavljene literature utvrditi prethodno nepoznate nuspojave, nadzirati poznate nuspojave, prepoznati nenadane rizike te prepoznati moguću sustavnu zlorabu ili uporabu izvan odobrene indikacije proizvoda FemoSeal™ VCS.

Najnoviji sustavni pregled literature, koji je obuhvatio razdoblje od 1. rujna 2019. do 31. kolovoza 2024., identificirao je 29 objavljenih studija koje su pružile podatke o kliničkoj sigurnosti i učinkovitosti FemoSeal™ VCS. Dvadeset i tri reference izvijestile su o upotrebi FemoSeal™ VCS-a u skladu s odobrenim indikacijama, a upotreba izvan odobrenih indikacija zabilježena je u devet studija. Općenito, pregledom literature ispitivanja specifičnih za uporabu sustava FemoSeal™ VCS utvrđena je populacija iz ispitivanja reprezentativna za bolesnike u EU-u podvrgnute perkutanim zahvatima vaskularne kateterizacije. Popis ovih 23 publikacija recenziranih od strane stručnjaka nalazi se u **dijelu 3**.

Klinička učinkovitost procijenjena je sljedećim mjerama:

- Vrijeme do hemostaze je bolje ili usporedivo s najsuvremenijim postupcima perkutanog zatvaranja zajedničke femoralne arterije.
- Vrijeme do pokretanja je bolje ili usporedivo s najsuvremenijim metodama perkutanog zatvaranja zajedničke femoralne arterije.
- Stopa postoperativnih komplikacija usporediva je ili niža od trenutanih standarda skrbi.

Na temelju tih kliničkih mjera učinkovitosti, prema podacima iz tog pregleda literature utvrđeno je da se sustav FemoSeal™ VCS može uspješno upotrebljavati pri zatvaranju femoralne arterijske punkcije (arteriotomija) u pacijenata podvrgnutih perkutanoj kateterizaciji s pomoću uvodne ovojnice od 7 Fr ili manje. Potpuna hemostaza postignuta je u većine bolesnika (79,65-100%) slučajeva i bila je povezana s medijanom vremena do hemostaze od 0,5 min, srednjim vremenom do otpusta od 3 dana. Između 69,2 i 86,7 % pacijenata moglo je hodati 5 sati nakon zatvaranja, uz prosječni postoperativni odmor od 349 minuta. Zatajenje sustava FemoSeal™ VCS uočeno je u 3,68 - 4 % slučajeva, a dodatna ručna kompresija bila je potrebna u 0,9 - 4,4 % postupaka.

Klinička sigurnost procijenjena je na temelju štetnih događaja, uključujući među ostalim:

- Krvarenje
- Hematom
- Pseudoaneurizma
- Modrice
- Arterijsko-venska fistula
- Infekcija
- Smrt

Za svaki od tih štetnih događaja učestalost pojave kod sustava FemoSeal™ VCS u obuhvaćenim ispitivanjima bila je manja ili usporediva s povijesno prijavljenim učestalostima za ručnu kompresiju i druge proizvode za zatvaranje krvnih žila.

Nisu utvrđeni nikakvi štetni događaji pregledom 10 izvještaja o slučajevima jer nisu utvrđeni nikakvi novi, nepredvidivi, nepoznati ni neprihvatljivi rizici.

Ukupna učinkovitost korištenja FemoSeal™ VCS-a tijekom dijagnostičke angiografije ili intervencijskih operacija ovisi o više čimbenika kao što su: spol, dob, anatomija pacijenta, komorbiditeti, anatomske položaj mjesta uboda, iskustvo kirurga, metoda postavljanja VCD-a, postoperativna njega itd. Osim tehničkog uspjeha, uključujući postizanje hemostaze, sustav FemoSeal™ VCS nudio je i kliničke koristi u odnosu na zatvaranje krvnih žila nakon punkcije femoralne arterije, kao što je smanjenje vremena do hemostaze, smanjenje vremena do pokretljivosti. Rezultati performansi za FemoSeal™ VCS sukladni su onima koji se očekuju za

ovu vrstu uređaja kada se koristi prema namjeni. Neki od referencija dobivenih tijekom trenutačnog razdoblja pretraživanja pokazali su upotrebu predmetnog uređaja na anatomskom mjestu koje nije zajednička femoralna arterija i za zatvaranje arteriotomija  $> 7$  Fr, što se smatra izvan oznake.

Tijekom pregleda nisu utvrđene nepoznate nuspojave, novi rizici ili moguća sustavna zlouporaba uređaja. Međutim, ako sustav FemoSeal™ VCS pažljivo upotrebljavaju obučeni liječnici, medicinski proizvod funkcionira kao koristan i potreban klinički proizvod. Općenito, ciljana terapija, a time i sustav FemoSeal™ VCS, rješava kliničku potrebu koja trenutačno postoji u liječenju komplikacija povezanih s vaskularnim pristupom.

Općenito, podacima u ovom pregledu literature nisu identificirani nikakvi problemi u vezi s učinkovitosti ni sigurnosti u kliničkom okruženju koji su prethodno bili nepoznati, kao ni štetni događaji čija je učestalost viša od predviđene/prihvatljive. Stoga se na temelju tog pregleda literature može zaključiti da sustav FemoSeal™ VCS, kada se upotrebljava za omogućavanje kompresije hemostaze kod arteriotomije nakon perkutane kateterizacije, nastavlja funkcionirati kako se očekuje i nije povezan s ozbiljnim sigurnosnim događajima.

#### 1.4.5 Sažetak podataka nakon stavljanja u promet

Uspostavljen je proaktivni sustav za nadzor nakon stavljanja u promet (engl. Post-Market Surveillance, PMS), a pregled svih pritužbi obavlja se na mjesečnoj osnovi i u skladu s internim proizvodnim postupcima. Podaci o prigovorima analizirani su u razdoblju od 1. rujna 2019. do 31. kolovoza 2024. Ukupno je proizvođaču podneseno 28 izvješća o nadzoru medicinskih proizvoda (MDV) i 476 izvješća o pritužbama kupaca. Od 28 izvješća o MDV-u, 27 je bilo povezano sa štetnim događajima, a jedno s kvarom uređaja. Tijekom izvještajnog razdoblja došlo je do dvije smrti, ali nije procijenjeno da je nijedna od prijavljenih smrti povezana s ispitanim proizvodom. Među 476 pritužbi podnesenih proizvođaču, najčešći razlozi za pritužbe bile su poteškoće s implementacijom (146 slučajeva, stopa pojavljivanja 0,0142%). Način kvara uzrokovan izvlačenjem je drugi najčešći sa stopom od 0,0126% (130 događaja).

FemoSeal™ sustav za zatvaranje krvnih žila ima preko 1.030.136 prodaja diljem svijeta i 827.843 u Europskom gospodarskom prostoru. Izračunata učestalost pritužbi na temelju globalne prodaje iznosi 0,043%. Ukupna stopa pritužbi kupaca vrlo je niska. Nisu utvrđeni nikakvi novi rizici koji već nisu uključeni u uputama za uporabu i dokumentaciji o rizicima.

Stope pojave neželjenih nuspojava prikazane su u **Tablici 1.2**. U pritužbama nisu utvrđeni novi nepredviđeni, nastali ili neprihvatljivi rizici. Nije došlo do značajnog povećanja učestalosti ili težine poznatih neželjenih nuspojava.

#### 1.4.6 Opći sažetak kliničke učinkovitosti i sigurnosti

Sustav FemoSeal™ VCS indiciran je za uporabu kod zatvaranja punkcije zajedničke femoralne arterije (arteriotomije) u pacijenata podvrgnutih perkutanoj kateterizaciji s pomoću uvodne ovojnice od 7 F (2,33 mm) ili manje. Ova klinička procjena temelji se na sveobuhvatnoj analizi dostupnih kliničkih podataka i literature, koji su relevantni za predviđenu namjenu proizvoda FemoSeal™ VCS, prije i nakon stavljanja u promet.

Proveden je sveobuhvatan pregled objavljene literature koji obuhvaća razdoblje od 1. rujna 2019. do 31. kolovoza 2024. Skup dokaza obuhvaćao je 29 ispitivanja sustava FemoSeal™ VCS. Iz dokaza pruženih u kliničkoj procjeni može se zaključiti da je predmetni proizvod siguran i učinkovit kada se upotrebljava u skladu s indikacijama te da su svi rizici ili neželjene nuspojave koji mogu biti povezani s proizvodom u normalnim uvjetima upotrebe prihvatljivi s obzirom na koristi za pacijenta. Ishodi izvedbe predmetnih proizvoda dosljedni su onima koji se očekuju za ovu vrstu uređaja kada se oni upotrebljavaju u skladu s namjenom.

Potencijalne neželjene nuspojave povezane s uporabom sustava FemoSeal™ VCS obuhvaćaju nuspojave koje se obično prijavljuju u vezi s alternativnim načinima zatvaranja arteriotomije, npr. krvarenje i hematoma. Sveukupno, stope učestalosti štetnih događaja prijavljenih uz uporabu sustava FemoSeal™ VCS slične su stopama prijavljenima za ručnu kompresiju i slične proizvode za zatvaranje krvnih žila. Konkretno, stope učestalosti za krvarenje i hematoma prijavljene za sustav FemoSeal™ VCS manje su od prijavljenih stopa za slične proizvode za zatvaranje krvnih žila. Svaki prijavljeni štetni događaj, i iz objavljene literature i na temelju praćenja nakon stavljanja u promet, prethodno je bio utvrđen (pogledajte **dio 1.3**).

Postojeći podaci o kliničkoj sigurnosti i učinkovitosti uređaja FemoSeal VCS upućuju na to da koristi za pacijenta od korištenja ovog uređaja za zatvaranje krvnih žila nadmašuju moguće rizike kada se koristi u skladu s Uputama za uporabu.

Kao što je naznačeno u prethodnim dijelovima, podaci dostavljeni za FemoSeal™ VCS pokazuju dosljednost između podataka vezanih uz uređaj koji se procjenjuje (npr. korištenje uređaja, sigurnosni ishodi, klinička učinkovitost i kliničke koristi), identificiranih ekvivalentnih uređaja i podataka vezanih uz slične uređaje navedene u dokumentu o trenutnom stanju tehnike.

Unakrsna analiza sigurnosnih podataka nije utvrdila nikakve razlike između sljedećeg:

- podataka spomenutih u najnovijim dostignućima
- podataka specifičnih za uređaj koji se procjenjuje
- podataka spomenutih u datotekama upravljanja rizikom
- podataka navedenih na oznakama i/ili u uputama za upotrebu (tj. obrađuju se preostali rizici koji se moraju prenijeti korisniku).



Klinička sigurnost dokazana je niskim stopama komplikacija utvrđenim u objavljenj, pregledanoj kliničkoj literaturi, kliničkim studijama koje je sponzorirala tvrtka, pregledu podataka nakon stavljanja na tržište, uz istovremeno odsustvo povlačenja proizvoda s tržišta. Nisu utvrđene nikakve zabrinutosti u vezi s učinkovitošću, pregledana literatura sadržavala je upotrebu FemoSeal™ VCS koja je bila u skladu s namjenom proizvođača..

### **1.5 Moguće dijagnostičke ili terapijske alternative**

Ručna kompresija tradicionalno se upotrebljava za postizanje hemostaze na mjestu arteriotomije nakon vaskularnih kateterizacija. Ručna kompresija povezuje se s duljom imobilizacijom pacijenta (do 8 sati nakon postupka) te sa znatnom nelagodom i produženim boravakom u bolnici. Nedavnim sustavnim pregledom utvrđeno je da je srednje vrijeme za postizanje hemostaze uz ručnu kompresiju bilo 20,8 minuta.<sup>1</sup>

Alternative ručnoj kompresiji obuhvaćaju vanjske hemostatske proizvode koji primjenjuju mehaničku kompresiju na mjesto arteriotomije. Ti proizvodi ne skraćuju vrijeme do hemostaze ni vrijeme do pokretljivosti, ali smanjuju potrebe osoblja zamjenom ručne kompresije mehaničkom kompresijom. Stope učestalosti štetnih događaja povezanih s upotrebom mehaničke kompresije slične su stopama kod ručne kompresije.

Proizvodi za zatvaranje krvnih žila, kao što je sustav FemoSeal™ VCS, dizajnirani su za zatvaranje arteriotomije. Cilj im je smanjiti vrijeme do hemostaze i omogućiti raniju pokretljivost. Nedavnim sustavnim pregledom, uključujući 13 komercijalno dostupnih proizvoda, utvrđeno je da je srednje vrijeme za postizanje hemostaze s proizvodom za zatvaranje krvnih žila iznosilo 5,4 minute. Medijan vremena do postizanja hemostaze za pojedinačne proizvode za zatvaranje krvnih žila u rasponu je od 1 minute (sustav FemoSeal™ VCS) do 14 minuta, dok je većina proizvoda između 4 i 10 minuta.<sup>1</sup>

Najčešće zabilježeni štetni događaji povezani sa zatvaranjem mjesta arteriotomije, s ručnim kompresijama, vanjskim hemostatskim proizvodima ili proizvodima za zatvaranje krvnih žila, obuhvaćaju hematome, krvarenje na mjestu pristupa, pseudoaneurizme, arteriovenske fistule i infekcije. Isti sustavni pregled (34 randomizirana kontrolirana ispitivanja, 14.401 pacijent) otkrio je da su stope štetnih događaja bile slične između ručne kompresije i uporabe proizvoda za zatvaranje krvnih žila, uz iznimku da je krvarenje bilo malo veće kod proizvoda za zatvaranje krvnih žila.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015.). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Predloženi korisnički profil i obuka

Predviđeni su korisnici sustava FemoSeal™ Vascular Closure System liječnici koji su završenom obukom kvalificirani za obavljanje arterijskog pristupa i zatvaranja u okviru endovaskularnih zahvata kroz zajedničku femoralnu arteriju te koji su sudjelovali u programu obuke za liječnike za FemoSeal™ društva Terumo Medical Corporation.

## 1.7 Relevantne usklađene i zajedničke norme

| Referentna norma | Trenutačna godina usklađenosti/rev. | Opis                                                                                                                                     |
|------------------|-------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070        | 2014/AMD1:2018                      | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070     | 2014/A1:2018                        | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance     | 20. svibnja 2021.                   | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052       | 2015                                | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213       | 2017                                | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503       | 2020                                | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182       | 2019                                | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |
| EN ISO 13485     | 2016/A11:2021                       | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 13485        | 2016                                | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |

| Referentna norma | Trenutačna godina usklađenosti/rev. | Opis                                                                                                                                                                     |
|------------------|-------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14644-1      | 2015                                | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1   | 2015                                | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2      | 2015                                | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2   | 2015                                | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3      | 2019                                | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3   | 2019                                | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1      | 2003                                | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1   | 2003                                | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2      | 2003/TC1:2004                       | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| EN ISO 14698-2   | 2003/TC 1:2004                      | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| USP <788>        | N/P                                 | PARTICULATE MATTER IN INJECTIONS                                                                                                                                         |

| Referentna norma         | Trenutačna godina usklađenosti/rev. | Opis                                                                                                                 |
|--------------------------|-------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| Farmakopeja EU-a 2.9.19. | NP                                  | Particulate Contamination: Sub-Visible Particles                                                                     |
| IEC 62366-1              | 2015                                | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN 62366-1               | 2015                                | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN ISO 14971             | 2019/A11:2021                       | Medical devices — Application of risk management to Medical devices                                                  |
| ISO 14971                | 2019                                | Medical devices — Application of risk management to Medical devices                                                  |
| ASTM F1980               | 2016                                | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1           | 2020                                | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1              | 2018                                | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2           | 2006.                               | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2              | 2006.                               | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3           | 2014                                | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3              | 2014                                | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4           | 2017                                | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4              | 2017                                | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |

| Referentna norma | Trenutačna godina usklađenosti/rev. | Opis                                                                                                                                       |
|------------------|-------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-5   | 2009                                | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                                         |
| ISO 10993-5      | 2009                                | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                                         |
| EN ISO 10993-6   | 2016                                | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| ISO 10993-6      | 2016                                | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| EN ISO 10993-10  | 2023                                | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| ISO 10993-10     | 2021                                | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| EN ISO 10993-11  | 2018                                | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| ISO 10993-11     | 2017                                | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| EN ISO 10993-12  | 2021                                | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| ISO 10993-12     | 2021                                | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| EN ISO 10993-17  | 2009                                | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17     | 2002.                               | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18     | 2020/A1:2022                        | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |

| Referentna norma | Trenutačna godina usklađenosti/rev. | Opis                                                                                                                                                                         |
|------------------|-------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-18  | 2020/A1:2022                        | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-23  | 2021                                | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23     | 2021                                | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382       | 2018                                | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756        | 2017                                | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>         | NP                                  | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>        | NP                                  | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72   | 2019                                | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135     | 2014/A1:2019                        | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135        | 2014/A1:2018                        | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7   | 2008/A1:2022                        | Biological evaluation of medical devices — Part 7: Ostatci sterilizacije etilen-oksidom                                                                                      |

| Referentna norma | Trenutačna godina usklađenosti/rev. | Opis                                                                                                                                                            |
|------------------|-------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-7      | 2008/A1:2019                        | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                               |
| EN 556-1         | 2024                                | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices |
| EN ISO 11737-1   | 2018/A1:2021                        | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11737-1      | 2018/A1:2021                        | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| EN ISO 11138-1   | 2017                                | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-1      | 2017                                | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| EN ISO 11138-2   | 2017                                | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 11138-2      | 2017                                | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| EN ISO 15223-1   | 2016                                | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| ISO 15223-1      | 2016                                | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| EN 1041          | 2008/A1:2013                        | Information supplied by the manufacturer of medical devices                                                                                                     |

| Referentna norma  | Trenutačna godina usklađenosti/rev. | Opis                                                                                                                                                                       |
|-------------------|-------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 11607-1    | 2020/A1:2023                        | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| ISO 11607-1       | 2019/A1:2023                        | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| EN ISO 11607-2    | 2020/A1:2023                        | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ISO 11607-2       | 2019/A1:2023                        | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169        | 2016                                | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M | 2016                                | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825        | 2018                                | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096        | 2011 (R 2019)                       | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M     | 2015                                | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021.-24     | 2021                                | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3       | 2020                                | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |



| Referentna norma | Trenutačna godina usklađenosti/rev. | Opis                                                                                                                                                                                               |
|------------------|-------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-8      | 2020                                | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                                                     |
| MDCG 2020-7      | 2020                                | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                                                  |
| MDCG 2020-6      | 2020                                | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                                               |
| MDCG 2019-9 v1   | 2022.                               | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                           |
| MDCG 2019-8 v2   | 2020                                | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                 |
| MDCG 2020-15     | 2020                                | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                           |
| MDCG 2021-11     | 2021                                | Guidance on Implant Card – ‘Device types’                                                                                                                                                          |
| MDCG 2021-19     | 2021                                | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                            |
| MDCG 2018-1 v4   | 2021                                | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                     |
| MDCG 2019-2      | 2019                                | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                 |
| MDCG 2019-1      | 2019                                | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                 |
| MDCG 2018-7      | 2018                                | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro |

| Referentna norma     | Trenutačna godina usklađenosti/rev. | Opis                                                                                                                                                                                          |
|----------------------|-------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                      |                                     | Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR))                                                                                                                                    |
| MDCG 2018-6          | 2018                                | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746   |
| MDCG 2018-4          | 2018                                | MDCG 2018-4 Annex: UDI database<br>Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                               |
| MDCG 2018-3 v1       | 2020                                | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25         | 2021                                | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2,12-2 Rev. 2 | 2012                                | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                        |

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### 3.0 POVIJEST REVIZIJE

| Broj revizije sažetka o sigurnosnoj i kliničkoj učinkovitosti | Datum izdanja      | Opis izmjene                                                      | Reviziju potvrdilo prijavljeno tijelo                                                                                                                                                                                                                                                                                                                                                                                    |
|---------------------------------------------------------------|--------------------|-------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022                                                  | 20. siječnja 2023. | Prvo izdanje, nakon CE certificiranja prema MDR-u                 | <input checked="" type="checkbox"/> Da<br>Jezik na kojem je provedena provjera: English<br><input checked="" type="checkbox"/> Ne (vrijedi samo za proizvode za implantaciju razreda IIa ili neke proizvode razreda IIb (MDR, članak 52., stavak 4., 2. odlomak) za koje sažetak o sigurnosnoj i kliničkoj učinkovitosti još nije potvrđen od strane prijavljenog tijela)<br><input type="checkbox"/> Drugo (objasnite): |
| SSCP-FS-2023 – revizija 1                                     | 15. ožujka 2024.   | Ažurirano za razdoblje od 1. siječnja 2019. do 31. prosinca 2023. | <input checked="" type="checkbox"/> Da<br>Jezik na kojem je provedena provjera: English<br><input type="checkbox"/> Ne (vrijedi samo za proizvode za implantaciju razreda IIa ili neke proizvode razreda IIb (MDR, članak 52., stavak 4., 2. odlomak) za koje SSCP još nije potvrđen od strane prijavljenog tijela)<br><input type="checkbox"/> Drugo (objasnite):                                                       |
| SSCP-FS-2024<br>Revizija 1                                    |                    | Ažurirano za razdoblje od 1. rujna 2019. do 31. kolovoza 2024.    | <input type="checkbox"/> Da<br>Jezik na kojem je provedena provjera: English<br><input type="checkbox"/> Ne (vrijedi samo za proizvode za implantaciju razreda IIa ili neke proizvode razreda IIb (MDR, članak 52., stavak 4., 2. odlomak) za koje                                                                                                                                                                       |

|                            |               |                                                   |                                                                                                                                                                                                                                                                                                                                                                            |
|----------------------------|---------------|---------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                            |               |                                                   | SSCP još nije potvrđen od strane prijavljenog tijela)<br><br><input type="checkbox"/> Drugo (objasnite):                                                                                                                                                                                                                                                                   |
| SSCP-FS-2024<br>Revizija 2 | June 20, 2025 | Revidirano na temelju upita NSAI-ja za validaciju | <input checked="" type="checkbox"/> Da<br>Jezik na kojem je provedena provjera: English<br><br><input type="checkbox"/> Ne (vrijedi samo za proizvode za implantaciju razreda IIa ili neke proizvode razreda IIb (MDR, članak 52., stavak 4., 2. odlomak) za koje SSCP još nije potvrđen od strane prijavljenog tijela)<br><br><input type="checkbox"/> Drugo (objasnite): |

**A biztonságosságra és a klinikai teljesítőképességre  
vonatkozó összefoglaló**

**FemoSeal™ Vascular Closure System**

|                                                               |                                                                                                             |
|---------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------|
| <b>Gyártó</b>                                                 | TERUMO MEDICAL CORPORATION<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 USA                         |
| <b>Gyártó egyedi regisztrációs<br/>száma (SRN)</b>            | US-MF-000019594                                                                                             |
| <b>Vezetőségi képviselő/PRRC</b>                              | Kimberly Feitl<br>Vice President, Quality                                                                   |
| <b>Alap UDI-DI</b>                                            | 38970FS79                                                                                                   |
| <b>EMDN-szám</b>                                              | C900199 - Haemostasis rendszerek-Egyéb                                                                      |
| <b>Készülék kategória</b>                                     | III. osztály                                                                                                |
| <b>Az év, amikor az eszköz<br/>először CE-jelölést kapott</b> | 2005                                                                                                        |
| <b>EK-képviselő</b>                                           | Terumo Europe N.V.<br>interleuvenlaan 40, 3001 LEUVEN, BELGIUM<br>Leuven<br>Belgium<br>SRN: BE-AR-000001433 |
| <b>Kijelölt testület</b>                                      | NSAI<br>CE 0050                                                                                             |



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A biztonságosságra és klinikai teljesítőképességre vonatkozó összefoglaló (SSCP) célja, hogy nyilvánosan hozzá lehessen férni a FemoSeal™ Vascular Closure System biztonságosságára és klinikai teljesítőképességére vonatkozó fő aspektusok frissített összefoglalójához.

Az alábbiakban a felhasználóknak/egészségügyi szakembereknek szánt eszköz biztonságosságát és klinikai teljesítőképességét összegezzük, lásd **1.0 szakasz**

## **1.0 ÖSSZEGZÉS FELHASZNÁLÓKNAK/EGÉSZSÉGÜGYI SZAKEMBEREKNEK**

Az SSCP nem helyettesíti a Használati útmutatót, amely az eszköz biztonságos használatáról szóló elsődleges dokumentum, és nem célja diagnosztikai vagy terápiás javaslatok nyújtása a célfelhasználóknak és betegeknek. Az SSCP nem helyettesíti az implantátumkártyákon vagy más kötelező dokumentumokban található kötelező információkat.

### **1.1 Az eszköz rendeltetésszerű használata**

#### **1.1.1 Rendeltetés**

A FemoSeal™ Vascular Closure System egy olyan orvosi eszköz, amely az artériás punkció lezárására szolgál a közös combartérián keresztüli perkután katéterezés után.

#### **1.1.2 Felhasználási javallatok**

A FemoSeal™ Vascular Closure System használata a közös combartéria-punkció (arteriotomia) lezárására javallott olyan betegeknél, akik 7F (2,33 mm) vagy kisebb bevezetőhüvely segítségével perkután katéterezéssel estek át.

#### **1.1.3 Ellenjavallatok és/vagy korlátozások**

A FemoSeal™ Vascular Closure System ellenjavallott olyan betegeknél, akiknél az arteriotomiák során 7F-nél (2,33 mm) nagyobb hüvelyt vagy eszközt használtak.

#### **1.1.4 Tervezett betegpopuláció**

A FemoSeal™ Vascular Closure System biztonságosságát és hatékonyságát 18 éves és idősebb betegeknél állapították meg, akik 7F (2,33 mm) vagy kisebb bevezetőhüvely alkalmazásával perkután katéterezéssel estek át.

#### **1.1.5 Különleges betegcsoportok**

A FemoSeal™ Vascular Closure System biztonságosságát és hatásosságát az alábbi betegpopulációkban nem igazolták:

- Fennálló autoimmun betegségben szenvedő betegek.
- Terápiás trombolízisben részesülő betegek.
- Klinikailag jelentős perifériás érbetegségben szenvedő betegek.
- Kontrollálatlan hipertónia ( $> 220$  Hgmm szisztolés vagy  $> 110$  Hgmm diasztolés) esetén.
- Vérzési zavarban szenvedő betegek, beleértve a thrombocytopeniát ( $< 100\,000$  trombocitaszám) vagy anaemiát (Hgb  $< 10$  mg/dl).

- Azon betegek, akiknél a közös combartéria belső lumene 5 mm-nél kisebb.
- Vese- vagy májkárosodásban szenvedő betegek.
- Egyéb releváns társbetegségben szenvedő betegek.
- Specifikus rasszhoz tartozó és/vagy etnikai származású betegek.
- Myocardialis infarktusból szenvedő betegek 72 órán belül.
- Ér-grafttal vagy sztenttel rendelkező betegek a punkció helyén.
- Terhes vagy szoptató betegek.
- 18 év alatti betegek.

### 1.1.6 Célfelhasználók

A FemoSeal™ Vascular Closure System tervezett felhasználói azok az orvosok, akik a közös combartérián keresztül képesek elvégezni az artériás hozzáférést és az endovaszkuláris eljárások lezárását, és részt vettek a Terumo Medical Corporation FemoSeal™ orvosoknak szóló oktatásán.

## 1.2 Az eszköz leírása

### 1.2.1 Az eszköz leírása

A Terumo Medical Corporation (TMC) által gyártott FemoSeal™ Vascular Closure System egy felszívódó érlezáró eszköz, amelyet arra terveztek, hogy a közös combartérián keresztüli perkután katéterezést követően combartériás vérzéscsillapítást érjen el.

A FemoSeal™ záróelemek két felszívódó polimer korongból, a belső tömítőkorongból és a külső zárókorongból állnak, amelyeket egy felszívódó sodrott fonal (multifilamentum) tart össze, ezáltal mechanikusan zárva az arteriotómiát. (lásd **1.1 ábra** és **1.2 ábra**) A kónusz burkolóhévelyén keresztül történő behelyezés után a külső rögzítőkorongot rá kell ütni a multifilamentum szára, ami a punkció helyének mechanikus lezárását eredményezi a belső és a külső zárólemez között. A belső és a külső zárókorongot a sodrott fonal tengely súrlódása tartja a helyén. A vérzéscsillapítás mechanikus eszközökkel érhető el. A záróelemek hidrolízis hatására elhasználódnak.

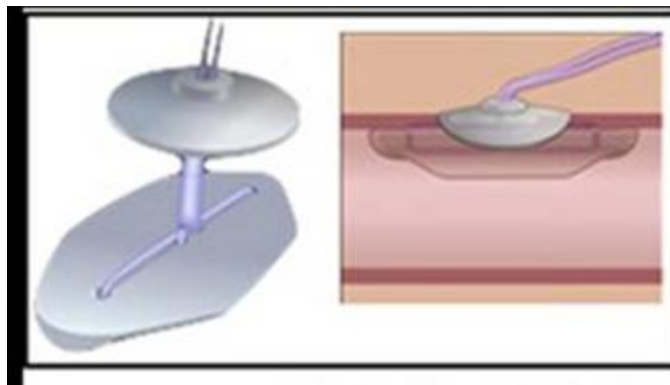
A beültethető zárókomponensek, a belső tömítés és a külső zárókorong tizennyolc (18) hónapon belül lebomlanak, míg a multifilamentum lebomlik és hidrolízissel felszívódik a környező szövetekben a becslések szerint két (2) - három (3) év után. A beültethető zárókomponenseknek az arteriotómián belüli kompresszió fenntartására való képességét nyolc (8) órán át vizsgálták. A

bomlástermékek a vizeletben metabolizálódnak és kiválasztódnak, vagy a tüdőkön keresztül szén-dioxid formájában kilégzésre kerülnek. Állatkísérletek során nem figyeltek meg felhalmozódásos hatásokat. A FemoSeal™ további összetevői, amelyek az eljárás során érintkeznek élő szövettel vagy vérrel, a kúp burkolóhüvelye, a tágitóeszköz, a tömítőcső, a tolóka és a vezetődrót.

### 1.1 ábra Belső tömítőkorong és külső zárókorong

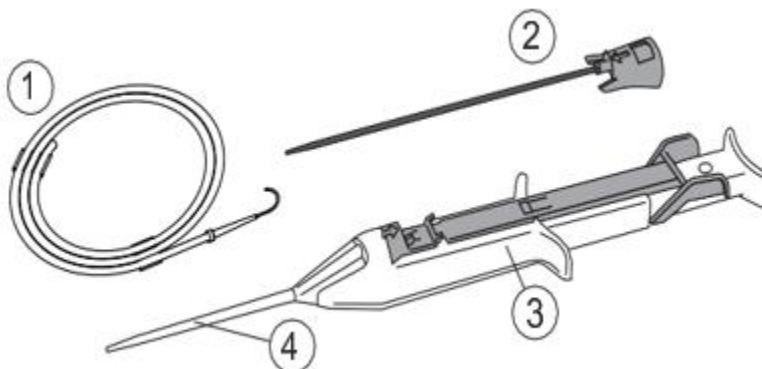


### 1.2 ábra. A belső tömítőkorong és a külső zárókorong behelyezve



A FemoSeal™ egység egy tágitóval és egy 0,038" (0,97 mm) külső átmérőjű, 27,5" (70 cm) hosszú vezetődróttal és egy J-egyenesítővel együtt kerül csomagolásra, lásd az alábbi, **1.3 ábrát**. A vezetődrót egy polietilén csőben található. Minden alkatrész egy rögzített papírtartó tálcába van csomagolva. A csomagolás tartalmazza a beteg implantátum kártyáját is. A FemoSeal™ Vascular Closure System nem igényel további kiegészítőket az eszköz rendeltetésszerű működéséhez, és az eszközt kizárólag a termék csomagolásában található tágitóval és vezetődróttal szabad használni.

### 1.3 ábra FemoSeal™ VCS egység vezetődórral és tágitóval



### 1.2.2 Nyersanyagok és összetevők

Az alábbi 1.1 táblázat ban a FemoSeal™ VCS komponenseinek listája látható.

1.1 táblázat. FemoSeal™ VCS nyersanyagok és komponensek

| Akatrész száma | Leírás                                     |                                               | Anyagok                                                                                                                                                                       |
|----------------|--------------------------------------------|-----------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1              | 0,038" (0,97 mm) vezetődórt J-egyenestővel |                                               | Vezetődórt: Rozsdamentes acél (304)<br>J-egyenestő: Polipropilén, lila pigment<br>Kapocs: Polietilén<br>Csővezeték: Polietilén                                                |
| 2              | FemoSeal™ tágitó                           |                                               | Fejrész: Tetrahydrofuran, kék pigment, polibutylén-tereftalát (PBT)<br>Cső: Nagy sűrűségű polietilén (HDPE), fekete pigment<br>Kenőanyag: Szilikon Dow Corning 360            |
| 3/4            | FemoSeal egység                            | Fröccsöntött RD7 - Belső és külső zárókorong* | Kopolimer a glikolid, trimetilén-karbonát, ε-kaprolakton és a TMP között: trimetilolpropán (iniciátor)                                                                        |
|                |                                            | sodrott fonal (multifilamentum) *             | Szegmentált kopolimer L,L-laktid, trimetilén-karbonát, ε-kaprolakton és 1,3 propán-diol (iniciátor) között<br>A bevonat kopolimer a glikolid, ε-kaprolakton és L-lizin között |
|                |                                            | Tömítőcső                                     | Polipropilén                                                                                                                                                                  |

|  |  |                       |                                                 |
|--|--|-----------------------|-------------------------------------------------|
|  |  | Toló                  | 304V Rozsdamentes acél                          |
|  |  | Csúszka               | Polibutilén-tereftalát (PBT)                    |
|  |  | Burkolat              | Polibutilén-tereftalát (PBT)                    |
|  |  | Gomb                  | Polibutilén-tereftalát (PBT)                    |
|  |  | Gombfedél             | Polioximetilén (POM)/poliacetál kopolimer       |
|  |  | Hüvely                | Polibutilén-tereftalát (PBT)                    |
|  |  | Távtartó              | Polibutilén-tereftalát (PBT)                    |
|  |  | Kónusz                | Polipropilén                                    |
|  |  | Burkolat fedele       | Polibutilén-tereftalát (PBT)                    |
|  |  | Biztonsági retesz     | Polibutilén-tereftalát (PBT), kék pigment       |
|  |  | Hüvely fedele         | Polibutilén-tereftalát (PBT)                    |
|  |  | Csőtömítés            | Szilikon merevítés A 70                         |
|  |  | Burkolattömítés       | Szilikon merevítés A 50                         |
|  |  | Rugó                  | 302 Rozsdamentes acél                           |
|  |  | Kónusz burkolóhüvelye | Polipropilén<br>Szilikon Dow Corning 360, hexán |

\* Az eszköz beültethető része; a beültethető komponensek MR-biztosak

A FemoSeal™ VCS etilén-oxiddal (EO) van sterilizálva, és egyszer használatos orvostechnikai eszköz. A FemoSeal™ VCS eszköz kialakítása olyan, hogy nem használható fel újra.

### **Működés módja**

A FemoSeal™ VCS elősegíti a mechanikus vérzéscsillapítást azáltal, hogy beültethető záróelemeket helyez el a közös combartérián belül és kívül. A vérzést megakadályozó mechanizmust a punkció helyét lezáró belső tömítés és a belső tömítést a helyén tartó külső zárókorong biztosítja.

#### **1.2.3 Klinikai előny**

A FemoSeal™ VCS az alábbi klinikai előnyöket biztosítja a közös combartéria punkciót követő érlezárással szemben:

- A vérzéscsillapításra fordított idő csökken <sup>1</sup>
- Az ambulációra fordított idő csökkentése <sup>1</sup>



*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

#### **1.2.4 Előző generáció(k) vagy változatok**

- A FemoSeal™ VCS (#11200) első verzióját 2005-ben és 2006-ban értékesítették az európai piacon.
- A továbbfejlesztett behelyező rendszerrel rendelkező FemoSeal™ VCS (#11202) 2006. március 28-tól kapható a piacon.

#### **1.2.5 Az eszközzel együtt használandó tartozékok**

A FemoSeal™ egység egy tágitóval, egy 0,038" (0,97 mm) külső átmérőjű, 27,5" (70 cm) hosszú vezetődróttal és egy J-egyenesítővel van csomagolva. A vezetődrót a FemoSeal™ egység tartozéka. A J-egyenesítő a vezetődrót része, míg a tágitó a FemoSeal™ egység része. A vezetődrót az egyetlen figyelembe vett tartozék. A vezetődrót egy polietilén csőben található. Minden alkatrész egy rögzített papírtartó tálcába van csomagolva. A csomagolás tartalmazza a beteg implantátum kártyáját is. A FemoSeal™ Vascular Closure System nem igényel további kiegészítőket az eszköz rendeltetésszerű működéséhez, és az eszközt kizárólag a termék csomagolásában található tágitóval és vezetődróttal szabad használni.

#### **1.2.6 Az eszközzel együtt használandó egyéb eszközök és termékek**

A FemoSeal™ VCS nem igényel további eszközöket a rendeltetésszerű működéshez.

### **1.3 Kockázatok és figyelmeztetések**

#### **1.3.1 Fennmaradó kockázatok és nemkívánatos hatások**

A FemoSeal™ VCS használatából eredő fennmaradó kockázatok következményeként esetleg jelentkező ismert vagy előrelátható nemkívánatos események, sérülések és szövődmények felsorolása az **1.2 táblázatban** található. Az előfordulási arány a Kockázati dokumentáció elemzésén alapul, és a 2019. szeptember 1-től 2024. augusztus 31-ig tartó értékesítés utáni felügyeleti adatok alapján kerül kiszámításra. A FemoSeal™ VCS-nek nincsenek ismeretlen maradék kockázatai, és minden vonatkozó kockázatot kezeltek a Használati útmutató és a kockázatkezelési folyamat révén.

## 1.2 táblázat FemoSeal nemkívánatos események/szövődmények

| Ártalom                            | Előfordulási arány (%) | Mérséklő tényezők                                                                                                                                                                                          |
|------------------------------------|------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Allergiás reakció                  | 0,0000                 | A kockázatok lehető legnagyobb mértékű csökkentésére irányuló teendőket és terveket a termék tervezési jellemzői, a gyártási irányelvek, termékcímkézés és az orvosok képzésének megfelelően alkották meg. |
| Aneurizma                          | 0,0000                 |                                                                                                                                                                                                            |
| AV fistula                         | 0,0001                 |                                                                                                                                                                                                            |
| Vérvesztetés/vérzés                | 0,0280                 |                                                                                                                                                                                                            |
| Halál                              | 0,0002                 |                                                                                                                                                                                                            |
| Ecchymosis                         | 0,0000                 |                                                                                                                                                                                                            |
| Embólia                            | 0,0000                 |                                                                                                                                                                                                            |
| Idegentest-reakció                 | 0,0000                 |                                                                                                                                                                                                            |
| Hematóma                           | 0,0027                 |                                                                                                                                                                                                            |
| Vérzés                             | 0,0001                 |                                                                                                                                                                                                            |
| Fertőzés                           | 0,0002                 |                                                                                                                                                                                                            |
| Gyulladásos reakció                | 0,0000                 |                                                                                                                                                                                                            |
| Zsibbadás                          | 0,0000                 |                                                                                                                                                                                                            |
| Fájdalom                           | 0,0000                 |                                                                                                                                                                                                            |
| A beteg diszkomfort érzete         | 0,0004                 |                                                                                                                                                                                                            |
| Beavatkozási késedelem             | 0,0065                 |                                                                                                                                                                                                            |
| Pszeudoaneurizma                   | 0,0004                 |                                                                                                                                                                                                            |
| Retroperitoneális vérzés           | 0,0002                 |                                                                                                                                                                                                            |
| Szepszis                           | 0,0000                 |                                                                                                                                                                                                            |
| Tromboembólia                      | 0,0000                 |                                                                                                                                                                                                            |
| Trombózis                          | 0,0001                 |                                                                                                                                                                                                            |
| Érelzáródás/alsó végtagi ischaemia | 0,0002                 |                                                                                                                                                                                                            |
| Az ér perforációja                 | 0,0000                 |                                                                                                                                                                                                            |
| Érszöveti disszekció/laceráció     | 0,0003                 |                                                                                                                                                                                                            |

### 1.3.2 Figyelmeztetések és óvintézkedések

#### Figyelmeztetések

1. Ne használja fel a terméket, ha a csomagolás sérült, vagy ha a steril gát nem sérült.
2. Ne használja fel a lejáratí idő után – a biológíailag lebomló összetevők nem feltétlenül működnek megfelelően.
3. Ne használja a terméket, ha az sérültnek vagy hibásnak tűnik.
4. FemoSeal™ Vascular Closure System használata, ahol az bevezetőhüvely vagy a környező szövetek bakteriális szennyeződése fertőzést okozhat.
5. Ha gyanítható, hogy a poszterior artériás fal át lett szúrva, vagy több artéria-punkció történt, ne hagyatkozzon kizárólag a FemoSeal™ Vascular Closure Systemre az artériás vérzéscsillapítás eléréséhez. Alkalmazzon további manuális vagy mechanikus kompressziót.
6. Ha a punkció helye a combartéria bifurkációja közelében vagy attól disztálisan van, a FemoSeal™ Vascular Closure Systemet nem szabad használni, mivel fennáll a belső tömítés nem megfelelő elhelyezkedésének kockázata. Ez az esemény vérzési szövődményeket és/vagy a normál véráramlás megszakadását eredményezheti.
7. Ha a bemetszés helyén tartós artériás vérzés alakul ki, ne vágja el a multifilamentumot, amíg a vérzést el nem éri. Ha nem sikerül vérzéscsillapítást elérni, rögzítse a multifilamentumot steril sebkötözővel, és alkalmazzon kiegészítő kompressziót, amíg el nem éri a vérzéscsillapítást. Tartós artériás vérzés esetén jelentős vérzéses szövődmények léphetnek fel, amelyek a beteg sérülését vagy halálát okozhatják.
8. Ne használja a FemoSeal™ Vascular Closure Systemet, ha a punkció helye proximálisan helyezkedik el az inguinalis szalaghoz képest, mivel ez retroperitoneális hematómát eredményezhet.
9. A vérzés szempontjából nagyobb kockázatú betegek fokozott vérvesztést szenvedhetnek, ami transzfúziót tehet szükségessé.
10. Ha a belső korong leválík, ez trombotikus és/vagy embóliás eseményt okozhat.

#### Óvintézkedések

1. A FemoSeal™ Vascular Closure System behelyezését olyan orvosoknak kell elvégezniük, akik megfelelő képzettséggel rendelkeznek az eszköz használatában.
2. A FemoSeal™ Vascular Closure System alkalmazása előtt végezzen korlátozott mértékű combartériás angiogramot vagy ultrahangos vezérlésű combartériás punkciót.
3. Szakítsa meg az eljárást, ha:

- A közös combartéria lumenátmérője < 5 mm.
  - Stenosis és/vagy jelentős lepedék van jelen a közös combartéria-punkció helyén.
  - Az artériás punkció a combartéria bifurkációjánál vagy attól disztálisan történik.
  - Rendellenes ágak vagy érrendellenességek vannak jelen a közös combartéria-punkció helyén.
4. Ha bármilyen hematóma van jelen, különös gonddal kell eljárni a kónusz burkolóhüvelyének az artériába történő megfelelő bevezetése érdekében.
  5. Használjon egyfalas punkciós technikát. Ne szúrja át az artéria hátsó falát.
  6. FemoSeal™ Vascular Closure System használata esetén mindig steril technikát alkalmazzon.
  7. A FemoSeal™ Vascular Closure System kizárólag egyszer használatos, és semmilyen módon nem szabad újrasztelizálni vagy újra felhasználni. A FemoSeal™ egység úgy van kialakítva, hogy nem használható fel újra.
  8. Ha a belső tömítés váratlan ellenállásba ütközik, szakítsa meg az eljárást.
  9. A belső tömítés megfelelő elhelyezéséhez helyezze vissza hüvelykujját, hogy a gomb szabadon visszaugorhasson.
  10. Bizonyosodjon meg arról, hogy a FemoSeal™ egység kónusz burkolóhüvelyének hegye a bőr felszíne alatt van, mielőtt a külső zárókorongot elhelyezné. A külső rögzítőkorong véletlenül a bőr szintje fölé helyezhető az combartéria és a bőr szintje közötti rövid távolsággal rendelkező betegeknél.
  11. A megfelelő elhelyezéshez a behelyezés előtt bőrmetszésre lehet szükség.
  12. Ha a belső tömítés az artériában található, de nem lehet teljesen lenyomni a gombot és behelyezni a külső zárókorongot, műtétre lehet szükség a FemoSeal™ záróelemek eltávolításához.
  13. Ha 18 hónapon belül ugyanazon combartéria újbóli punkciójára van szükség, a punkciót az előző FemoSeal™ Vascular Closure System hozzáférési helyétől legalább egy centiméterre proximálisan kell elvégezni.
  14. Utasítsa a beteget, hogy kövesse a lezárás helyének vizsgálatára vonatkozó orvosi utasításokat.
  15. Utasítsa a beteget, hogy mindig tartsa magánál a betegtájékoztató kártyát a következő 18 hónapban.

## **Óvintézkedések az elbocsátáskor**

Az elbocsátás megfontolása előtt mérje fel a beteget a következő klinikai állapotok szempontjából:

1. Vérzés és/vagy hematóma a lezárás helyén.
2. Sétálás közben fájdalom.
3. Fertőzés jelei a lezárás helyén.

### **1.3.3 Helyszíni biztonsági korrekciós intézkedések**

2019. szeptember 01-től 2024. augusztus 31-ig egyetlen helyszíni biztonsági korrekciós intézkedés történt a FemoSeal™ VCS rendszer kapcsán.

2022-ben a Terumo önkéntesen visszahívta a FemoSeal™ VCS tömítőeszközt olyan panaszok miatt, amelyek szerint az Elkton gyártóüzemben készült termékeknél hibák fordultak elő a tömörítőerő és a visszahúzóerő mérésére szolgáló gyártási és tételfelszabadítási tesztek során. Összesen 950 egységet hívtak vissza Dél-Koreából.

## **1.4 A klinikai értékelés és a forgalomba hozatalt követő klinikai utánkövetés**

Az **1.3 táblázat** tartalmazza a kulcsfontosságú vizsgálatok listáját, amelyek a FemoSeal™ VCS forgalomba hozatalát, valamint a forgalomba hozatal utáni vizsgálatok és a forgalomba hozatalt követő klinikai utánkövetési tevékenységek bemutatását szolgálják. A vizsgálat során használt eszközverziót az alábbi táblázat tartalmazza. A FemoSeal™ VCS (#11200) első verziója 2006-ig volt jelen a piacon, míg a következő változat (#C11202) 2006-ban jelent meg a piacon, és jelenleg ez az, ami jelenleg a piacon van.

### **1.3 táblázat: A pivotális vizsgálatok összefoglalása**

| <b>Forgalomba hozatal előtti funkcionális állatkísérletek</b>                                                                                                                                                                                                           | <b>Eszközverzió</b> |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200               |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200               |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200               |
| <b>Első humánklinikai vizsgálat</b>                                                                                                                                                                                                                                     |                     |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200               |

| Elvégzett, forgalomba hozatal utáni klinikai vizsgálatok                                                                        |                             |
|---------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                      | C11202<br>(aktuális eszköz) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                               | C11202<br>(aktuális eszköz) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | C11202<br>(aktuális eszköz) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)          | C11202<br>(aktuális eszköz) |
| Tervezett / folyamatban lévő forgalomba hozatal utáni klinikai vizsgálatok                                                      |                             |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                      | C11202<br>(aktuális eszköz) |
| Forgalomba hozatal utáni klinikai utánkövetési tevékenységek                                                                    |                             |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(aktuális eszköz) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(aktuális eszköz) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(aktuális eszköz) |

### 1.4.1 A forgalomba hozatal előtti állatkísérletek és klinikai vizsgálatok adatainak összefoglalása

Az alábbi **1.4 táblázat** az összes forgalomba hozatal előtti vizsgálat leírását tartalmazza, mind az állatkísérletek, mind a klinikai vizsgálatok tekintetében.

**1.4. táblázat: A forgalomba hozatal előtti vizsgálatok összefoglalása**

| Forgalomba hozatal előtti funkcionális állatkísérletek                                                                                                                                                                                          |                                                                                |                                        |                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                               |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Vizsgálat neve                                                                                                                                                                                                                                  | Év / CI                                                                        | Vizsgálat típusa                       | Célkitűzések                                                                                                                                                                                                                                                                               | Mérföldkövek                                                                                                                                                                                                                                                | Lehetséges elfogadási kritériumok                                                                                                                                                                                                                                                                                                                                                                             |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculture System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed | 2000<br><br>Radi Medical System AB<br><br>Kivitelező: Biomatech, Franciaország | Állatkísérletek<br>; Feltáró vizsgálat | A vizsgálat célja egy olyan biológiailag lebomló implantátum biokompatibilitásának és biofunkcionalitásának értékelése volt, amelyet a vérzéscsillapítás elérésére terveztek az érrendszerben. A jelentésben a tartalék állatok jelentése a 862. sz. vizsgálatból (1051-01 sz. dokumentum) | N = 3 felnőtt nőstény juh, 1 állat időpontonként<br><br>Utánkövetés: kórszövettani elemzés, a makroszkopikus osztályozás és ultrastrukturális elemzés<br><br><ul style="list-style-type: none"> <li>12 hónap</li> <li>15 hónap</li> <li>18 hónap</li> </ul> | Artériás átjárhatóság <ul style="list-style-type: none"> <li>A beültetést követően a véráramlás értékelése - az ideiglenes, az eljárásnak tulajdonított érgörcshöz társuló 2/3-os véráramlás csökkenése, mindkettő a bal oldali közös carotis artériában fordult elő</li> <li>Szín doppler ultrahang vizsgálat (4 hét) - 3/3 (100%) nagyobb véráramlás-csökkenés nélkül 30 nappal a beültetés után</li> </ul> |

|                           |  |  |  |                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|---------------------------|--|--|--|-----------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| by Biomatech,<br>France). |  |  |  | Szín doppler ultrahang<br>utánkövetés – 30 nap a carotis és<br>combartériás hozzáférési<br>pontokon | <p>Makroszkópos megfigyelés</p> <ul style="list-style-type: none"> <li>• 12 hónap - az átjárhatóság makroszkopikusan igazolt, mivel nincs anatómiailag látható elzáródás; nincs makroszkopikus lokális intolerancia lézió (vérzés, nekrozis vagy neovascularizáció); a belső korong betokolódása megjelölendőnek tűnt</li> <li>• 15 hónap - a makroszkopikus megfigyelés nem mutatott gyulladást; a belső és külső korongok maradványait nem azonosították; a külső korong területén található beágyazott szövet a 12 hónapos megfigyeléssel megegyezőnek tűnt</li> <li>• 18 hónap - a makroszkopikus megfigyelés nem mutatott ki helyi intoleranciát, a külső korong látható volt (3/3 eset), a belső korong teljes lebomlását; 1/3 (bal oldali gyakori carotis artéria) - az implantátum helyén megfigyelt artéria fal depresszióját (az eszköz behelyezéséhez kapcsolódóan)</li> </ul> |
|                           |  |  |  |                                                                                                     | <p>Következtetés</p> <ul style="list-style-type: none"> <li>• Makroszkóposan, 12, 15 és 18 hónappal a beültetés után nem mutattak ki nekrotikus, degeneratív vagy trombózis jeleket.</li> <li>• A belső és a külső korongok lebomlási folyamata 12 és 18 hónap között alakult ki, és 18 hónap elteltével varrták le azokat, a beültetendő terület fehér szövet borítja.</li> <li>• Szövettanilag 18 hónap elteltével a polimer anyag már nem volt látható, de endoluminális rostos szövet volt jelen. Nem figyeltek meg</li> </ul>                                                                                                                                                                                                                                                                                                                                                        |

|                                                                                                                                                                                                                                                                         |                                                                         |                                    |                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                       | nekrotikus, degeneratív vagy trombózisos léziókat.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 2002 Radi Medical System AB<br><br>Kivitelező: Biomatech, Franciaország | Állatkísérletek; Feltáró vizsgálat | A vizsgálat célja egy biológiailag lebomló implantátum biológiai kompatibilitásának értékelése volt, amely az érrendszerben vérzéscsillapítást ér el. | Utánkövetés (beültetés után)<br><ul style="list-style-type: none"><li>• 12. hét</li><li>• 24. hét</li><li>• 36. hét</li></ul><br>N = 12 juh, 3 állat egy időpontra, 3 tartalék állat 12, 15 és 18 hónapra<br><br>Beültetési helyek - jobb és bal oldali combartériák, jobb és bal oldali közös carotis artériák<br><br>Szín doppler ultrahang elemzés | <u>A carotis és combartériák átjárhatósága 4 hét után</u><br><ul style="list-style-type: none"><li>• Fő véráramlás-csökkentés 0/12 (0%)</li></ul><br><u>Nincs jelentősebb véráramlás-csökkenés</u><br><ul style="list-style-type: none"><li>• Az eszköz behelyezésével kapcsolatos súlyos véráramlási zavarok 0/12 (0%)</li><li>• Véráramlás csökkenése a bal oldali közös carotis artériákban 2/12 (16,6%) az ideiglenes artériás vasospasmus miatt (a műtétre vonatkozik, nem az eszközre)</li></ul><br><u>Véráramlás romlása utánkövetéssel</u><br>12. hét - 0/12 (0%)<br>24. hét - 0/12 (0%)<br>36. hét - 0/12 (0%)<br><br>Vérnyomás mérések (3 juh – 36. hét)<br><ul style="list-style-type: none"><li>• Nem észlelhető jelentős véráramlás-csökkenés</li></ul><br>Makroszkopikus adatok az integrációhoz és a degradációhoz (0-4. fokozat)<br><br><u>Carotis helyek</u><br><u>Belső oldal</u><br>-tokosodás<br>12. hét 1,3<br>24. hét 0,8<br>36. hét 0,7<br>-anyaglebomlás<br>12. hét 2,2<br>24. hét 2,3<br>36. hét 0,7<br><u>Külső oldal</u><br>-tokosodás<br>12. hét 2,0 |



|  |  |  |  |  | 24. hét 1,0<br>36. hét, 0,8<br>-anyaglebomlás<br>12. hét 2,0<br>24. hét 2,7<br>36. hét 3,2<br><br><u>Combi hozzáférés</u><br><i>Külső oldal</i><br>-tokosodás<br>12. hét 1,0<br>24. hét 2,7<br>36. hét 1,0<br>-anyaglebomlás<br>12. hét 2,0<br>24. hét 2,4<br>36. hét 3,0<br><br><i>Belső oldal</i><br>-tokosodás<br>12. hét 2,0<br>24. hét 1,2<br>36. hét 1,0<br>-anyaglebomlás<br>12. hét 1,0<br>24. hét 2,2<br>36. hét 3,0<br><br><u>Szövetteni adatok az integrációhoz, a degradációhoz és a gyulladáshoz és a gyulladáshoz kapcsolódó paraméterekhez (a releváns értékek átlaga, 0-4-es index) n=6</u><br><br><u>Carotis helyek</u><br>Külső fibrózis<br>12. hét – 2,3<br>24. hét – 2,3<br>36. hét – 1,8<br>Belső neointima<br>12. hét – 3,0<br>24. hét – 2,7<br>36. hét – 3,3<br>Anyaglebomlás<br>12. hét – 1,7<br>24. hét – 3,0<br>36. hét – 3 +<br>Gyulladáshoz kapcsolódó paraméterek (makrofágok) |
|--|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | 12. hét – 3,0<br>24. hét – 1,7<br>36. hét – 1,7<br><u>Combi hozzáférés</u><br>Külső fibrózis<br>12. hét – 1,3<br>24. hét – 1,5<br>36. hét – 1,7<br>Belső neointima<br>12. hét – 3,7<br>24. hét – 3,3<br>36. hét – 3,8<br>Anyaglebomlás<br>12. hét – 2,0<br>24. hét – 3,0<br>36. hét – 3+<br>Gyulladásos paraméterek<br>(makrofágok)<br>12. hét – 3,5<br>24. hét – 1,8<br>36. hét – 1,8<br><br><u>Hisztomorfológiai</u><br><u>átjárhatósági értékek</u><br>Carotis helyek<br>12. hét 74,0%<br>24. hét 81,9%<br>36. hét–89,43%<br>Combi hozzáférés<br>12. hét – 42,2%<br>24. hét – 73,21%<br>36. hét – 78,71%<br><br><u>US ér átjárhatóság (átlag %)</u><br>Carotid hely<br>12. hét 94,6%<br>24. hét – 96,7%<br>36. hét – 94,7%<br>Combi hozzáférés<br>12. hét – 66,9%<br>24. hét – 63,6%<br>36. hét – 75,1%<br><br>Következtetés<br><ul style="list-style-type: none"> <li>Súlyos lokális<br/>intolerancia jele nem<br/>volt észlelhető (látható<br/>gyulladásos, nekrotikus<br/>vagy degeneratív léziók<br/>hiánya) 12, 24 vagy 36<br/>hét elteltével</li> </ul> |
|--|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                                                                                                                                                                                                                                                                 |                                                                                |                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
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|                                                                                                                                                                                                                                                                 |                                                                                |                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                   | <ul style="list-style-type: none"> <li>A gazdaszervezet és az eszköz tekintetében nem jelentettek szignifikáns csontmellékhatásokat</li> <li>Az implantátum lebomlása a 36. héten majdnem teljesen befejeződött</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France). | 2002<br><br>Radi Medical System AB<br><br>Kivitelező: Biomatech, Franciaország | Állatkísérletek | A vizsgálat célja egy olyan biológiailag lebomló implantátum biokompatibilitásának és biofunkcionalitásának értékelése volt, amelyet az érrendszerben vérvéscsillapítás elérésére terveztek. A vizsgált eszközt az artériák punkciós nyílásába történő bevezetésre tervezték a vérvéscsillapítás elérése érdekében. Az egyik korong az artéria punkciós nyílásába hatolt, a másik pedig az artérián kívülről megszorította a belső korongot. Mindkét korongot egy behelyezőhüvelyen keresztül vezették be. A korongokat úgy tervezték, hogy megakadályozzák a vézést, begyógyuljanak az érfalba, végül lebomoljanak és felszívódnak. A vizsgálat célja a funkcionális implantátum, juhba és sertésbe történő beültetése utáni adatgyűjtés és -elemzés az implantátum kapacitásának értékelése a fiziológias funkció fenntartása tekintetében a keringési rendszerben történő használat során, a gazdaszervezet, illetve és az eszköz választának (a fizikai integritás, szöveti tokosodás áldozatával ) | Az implantációs időszak / utánkövetés minden állat esetében 5 hét<br><br>4 juh, 1 sertés<br><br>14 záróelem<br><br>8 záróelem, 2 juhba ültetve,<br><br>2 záróelem, 1 sertésbe ültetve<br><br>Amikor két záróelemet beültetettek ugyanabba a combartériába, azokat > 30 mm távolságban ültették be | <p>A mellékhatásokat (gyulladás, nekrozis, vérzés vagy bármilyen más lézió) vagy a vékony pszeudo-intimális rétegeképződést feljegyezték. Különös figyelmet fordítottunk az eszköz kezdeti csontbeépítésére, különös tekintettel a korongok belső tokosodására.</p> <p>Makroszkóposan nem figyelték meg jelentős helyi intolerancia vagy trombusképződés jeleit. A makroszkopikus megfigyelés nem mutatott ki különbséget a juh és a sertés között a záróelemek combartériákba történő beültetése után.</p> <p>Makroszkóposan nem figyelték meg jelentős helyi intolerancia vagy trombusképződés jeleit. A makroszkopikus megfigyelés nem mutatott ki különbséget a juh és a sertés között a záróelemek combartériákba történő beültetése után.</p> <p>A juh implantációs hely hisztopatológiai elemzése nem mutatott ki helyi mellékhatásokat. A belső és a külső korongok a degradáció jeleit mutatták, és néhány esetben kisebb</p> |

|                                                                                                                                                                                                              |                              |                                                             |                                                                                                                                                                                                                               |                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                              |                              |                                                             | meghatározása és az implantátum degradálódásának értékelése.                                                                                                                                                                  |                                                                                                                                                                                          | <p>részekre törtek. A belső korongok teljesen be lettek építve a neointimális szövetbe. A sertésben a histopatológiai elemzés kissé több gyulladásos jelet mutatott a belső és a külső korongok körül. Mindkét állat esetében a multifilamentum a korong anyagához viszonyítva kissé több gyulladásos jelet mutatott, ami a nagyobb felület miatt normálisnak számít a fonott varratok esetében.</p> <p>Az ér átjárhatóságát 5 hét után, három különböző módszerrel mérték: hisztomorfometriával, az érátmérő tolómérő segítségével történő mérésével kombinált hisztomorfometriával, és szín doppler ultrahang vizsgálattal. Az ér átlagos átjárhatósága a juhokban 60 és 80% között volt, a módszertől függően (12 megfigyelés). A sertésben az ér átlagos átjárhatósága 40 és 80% között volt (2 megfigyelés).</p> |
| <b>Első humánklinikai vizsgálat</b>                                                                                                                                                                          |                              |                                                             |                                                                                                                                                                                                                               |                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| <b>Vizsgálat neve</b>                                                                                                                                                                                        | <b>Év / CI</b>               | <b>Vizsgálat típusa</b>                                     | <b>Célkitűzések</b>                                                                                                                                                                                                           | <b>Mérőföldkövek</b>                                                                                                                                                                     | <b>Lehetséges elfogadási kritériumok</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Nyílt, egykaros, több központban végzett klinikai vizsgálat | A vizsgálat célja a FemoSeal Vascular Closure System (FemoSeal System) biztonságosságának, teljesítőképességének és hatékonyságának megállapítása volt, különös tekintettel a záróelemekre azon betegeknél, akik combartéria- | 2 részes klinikai vizsgálat<br><br>Össz n = 80<br>1. rész n = 20<br>2. rész n = 60<br>Javallatok:<br>1. rész – Diagnosztikus szívkatéterezés combartériát használva hozzáférési helyként | Eredmények<br><br>-vérzéscsillapítás<br>kompresszió nélkül, FS-sel elérve<br><br>- 1. rész 20/20 (100%)<br>- 2. rész 58/60 (97%)<br><br>A vérzéscsillapításig eltelt medián idő a beavatkozás időpontjában (2. rész) – 1,0 perc (a tartomány azonnal – 8 perc)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |

|  |  |  | hozzáférést alkalmazó<br>szívdiagnosztikai vagy<br>intervenciós kardiológiai<br>eljárásokon estek át. | 2. rész – Diagnosztikus és<br>intervenciós szívűtéten áteső<br>betegek, akiknél combartériát<br>használtak hozzáférési helyként<br><br>30 napos utánkövetés | <u>Ambulációs idő (perc)</u><br>1. rész –<br>Medián: 33,0<br>átlag: 67,8<br>2. rész –<br>medián: 45<br>átlag: 87,5<br><br><u>Súlyos vaszkuláris<br/>szövődmények<br/>előfordulása – 30 napos<br/>utánkövetés</u><br>1. rész<br>-Érrendszeri<br>szövődményektől mentes<br>20/20 (100%)<br>2. rész<br>Pseudoaneurizma - 1/59<br>(1,69%)<br><br><u>Kezelési kudarc</u><br>1. rész – 0/20 (0%)<br>2. rész – 3/60 (5%) <ul style="list-style-type: none"> <li>2, ahol nem sikerül a<br/>vérzéscsillapítást<br/>kompressziós<br/>technika alkalmazása<br/>nélkül elérni</li> <li>1 súlyos vaszkuláris<br/>szövődmény miatt,<br/>pseudoaneurizma</li> </ul><br><u>Tartós nedvszivárgás</u><br>1. rész – 0/20 (0%)<br>2. rész – 8/60 (13%)<br><br><u>Hematóma</u><br>1. rész – 0/20 (0%)<br>2. rész – 6/60 rész (10%) |
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A FemoSeal™ VCS forgalomba hozatal előtti fejlesztési tervének részeként három állati funkcionális tesztet végeztek el. 2000-ben a klinikai vizsgálatok megkezdése előtt állatkísérletet végeztek a FemoSeal™ VCS biofunkcionalitásának értékelésére. Ez a vizsgálat értékelte a záróelemek képességét a fiziológiai funkció fenntartására és lebomlásának értékelésére. 18 hónap elteltével a belső és külső korong anyaga már nem volt látható, a helyét endoluminális rostos szövet vette át. Következésképpen a FemoSeal™ VCS záróelem azon kapacitása, amely fenntartja a fiziológiás funkciót, amikor a keringési rendszerben használják.

2002-ben állatkísérletet végeztek egy biológiailag lebomló implantátum, a FemoSeal™ VCS biokompatibilitásának és biofunkcionalitásának értékelésére, amelyet az érrendszerben vérzéscsillapítás elérésére terveztek. Összefoglalva, az implantátum lebomlása a 36. hétre csaknem befejeződött, és nem volt jelentős káros szöveti reakció.

Egy másik állatkísérlet 2002-ben vizsgálta egy biológiailag lebomló implantátum, a FemoSeal™ VCS biokompatibilitását és biofunkcionalitását, amelyet az érrendszerben vérzéscsillapítás elérésére terveztek 5 hét elteltével a korong teljes mértékben betokozódott, és a belső és külső korongok esetében degradáció jeleit figyelték meg. Következésképpen, az implantátum azon képessége, hogy megőrzi a fiziológiás funkciót, amikor a keringési rendszerben használják, igazolást nyert.

A FemoSeal™ VCS klinikai fejlesztési tervének részeként a Radi Medical System AB forgalomba hozatal előtti klinikai vizsgálatot végzett. Ez a klinikai vizsgálat nem jelent meg és nem érhető el online. A #11200 eszköztípussal végzett vizsgálatot 2002–2004-ben végezték az EN 540 európai szabvány (orvostechnikai eszközök humánklinikai vizsgálata) szerint, valamint az ICH klinikai vizsgálatokra vonatkozó általános megfontolások és a helyes klinikai gyakorlatra vonatkozó iránymutatás szerint. A vizsgálat részleteit az EU-SE-001 számú jelentésben dokumentálják. A klinikai vizsgálatot a Radi Medical Systems AB „Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures” című végső jelentésben dokumentálták. A klinikai vizsgálatot a FemoSeal™ első, #11200-as modelljével végezték, és a beültethető zárókomponensek biztonságosságára és hatásosságára összpontosítottak. Az egyetlen különbség az első #11200 modell és az aktuális C11202 modell között a francia méret, a 6F és a 7F, valamint a továbbfejlesztett bejuttató rendszer között. A klinikai előnyök, a rendeltetésszerű használat, a működtetés alapelvei és a beültethető záróelemek, a belső tömítés és a külső zárókorong nyersanyagai változatlanok maradnak.

Az eszköz használata diagnosztikai szív- vagy intervenciós szívsebészeti beavatkozásokon áteső betegeknél javallott, a combartériát hozzáférési pontként használva. A vizsgálat célja a FemoSeal™ VCS biztonságosságának, Teljesítőképességének és hatékonyságának meghatározása volt. Ez egy prospektív, többközpontú, egykaros, nyílt vizsgálat volt, 30 napos utánkövetéssel.

Az elsődleges teljesítmény végpont a vérzéscsillapításig eltelt idő volt, amelyet a vérzés hiányaként határoztak meg. Az elsődleges biztonsági végpont a jelentős vaszkuláris komplikációk előfordulása volt 30 napig. A másodlagos végpontok között szerepelt az ambulációhoz szükséges idő, a kezelési hibák részaránya, a nemkívánatos események előfordulása és az eszköz teljesítményjellemzői a bejuttatás és a behelyezés során.

A vizsgálatban részt vevő betegek olyan felnőttek voltak, akik tájékozott beleegyezést és legalább egy ép pedálimpulzust tudtak adni. A betegeket kizárták a vizsgálatból, ha a következő állapotok bármelyike fennáll:

- Korábbi perifériás érbetegségek
- Autoimmun betegség
- Ismert súlyos anaemia vérzési zavarai
- INR >1,5
- Miokardiális infarktus 72 órán belül
- A kezelés ellenére kontrollálatlan hipertónia
- Elhízás, amely kizárja a Seldinger technikával való hozzáférést
- Ér-graft vagy sztent jelenléte az arteriotómiás területen
- Korábbi ipsilaterális punkció 3 hónapon belül
- Várható élettartam < 6 hónap

Ezenkívül a betegeket műtét közben megvizsgálták, és kizárták a vizsgálatból, ha az alábbiak bármelyikét megfigyelték:

- A közös combartéria lumenátmérője <5 mm
- Artériás ágak a punkció helyétől 2 cm-re proximálisan
- Jelentős szűkület a punkció helyén belül 3 cm-en belül
- Az elsődleges bevezető katéterhüvely használata >6Fr
- Femorális bifurkációhoz képest disztálisan vagy középen végzett punkció
- Többszörös combi punkció
- Ismert vagy gyanított hátsó combartériás falpunkció
- Nagy hematóma (2:6 cm) az eljárás befejezésekor
- Az eljáráshoz az elsődleges hüvelybehelyezés nehéz a tekervényes szövet vagy ér miatt

Ezt az egyprotokollós vizsgálatot két részben végezték: 20 beteget vontak be az 1. részbe, majd biztonsági elemzést végeztek, majd további 60 beteget vontak be a 2. részbe.

Az 1. részben a bevont betegek átlagos életkora 65,9 év volt, a betegek 70,0%-a férfi volt, a betegek 95%-a pedig egyidejűleg gyógyszeres kezelésben részesült. A vizsgálat 2. részében az átlagos életkor 63,8 év volt, a 78% férfi volt, és 100%-ban egyidejűleg gyógyszeres kezelésben részesült.

A diagnosztikai (1. és 2. rész) vagy intervenciós (2. rész) szívkatóterezési eljárásokon áteső betegek a vizsgálatba bevonhatók voltak. Az eljárások megfeleltek a vizsgálatba bevont kórházak összességében előírt ellátási előírásainak, melyet a FemoSeal™ VCS használata követett. A betegadatokat a kiindulási értéknél, az eljárás során, valamint az 1 napos és 30 napos eljárás után gyűjtötték. Az eredmények az **1.5 táblázatban** vannak összefoglalva, és azt jelzik, hogy a FemoSeal™ VCS biztonságos és hatásos az adott betegpopulációban történő használatra.

**1.5 táblázat: A forgalomba hozatal előtti vizsgálatban jelentett klinikai eredmények**

|                                                                                                                                  | 1. rész   | 2. rész                |
|----------------------------------------------------------------------------------------------------------------------------------|-----------|------------------------|
| Betegek száma                                                                                                                    | 20        | 60                     |
| A vérzéscsillapítás átlagos ideje                                                                                                | 1,2 perc  | 1,6 perc <sup>a</sup>  |
| Ambulációig eltelt átlagos idő                                                                                                   | 72,2 perc | 87,5 perc <sup>b</sup> |
| Súlyos vaszkuláris szövődmények előfordulása <sup>c</sup>                                                                        | 0 (0%)    | 1 (2%)                 |
| Nemkívánatos eseményt mutató betegek száma                                                                                       | 5 (25%)   | 19 (32%)               |
| Kezelési kudarc (a meghatározás szerint: jelentős vaszkuláris szövődményként manuális kompresszió szükségessége, vagy mindkettő) | 0 (0%)    | 3 (5%)                 |
| Az eszköz hibás működés                                                                                                          | 0 (0%)    | 6 (10%)                |

<sup>a</sup> 58-as teljes mintaméret alapján, mivel 2 beteg nem érte el a vérzéscsillapítást az eljárás idején a korábbi ipsilaterális punkciók miatt. A vérzéscsillapítás ezen betegek esetében 7,37 percig tartott.

<sup>b</sup> 59-es teljes mintaméret alapján: 1 beteget nem vontak be, mivel a tüdőödéma miatt lélegeztetőgépre helyezték, és esetében egy hétnél hosszabb ideig nem volt elérhető az ambuláció.

<sup>c</sup> Meghatározás szerint: vérátömlesztést vagy műtéti korrekciót igénylő érkomplikáció, illetve olyan helyi fertőzés, amely antibiotikum adását, kórházi kezelést vagy kórházi kezelés meghosszabbítását vagy helyi sebtisztítást igényel



A vizsgálat 1. részében nem figyeltek meg nagyobb érrendszeri szövődményeket. A vizsgálat 2. részében 1 nagyobb érrendszeri szövődményről számoltak be: pszeudoaneurizmáról, amelyet a beavatkozást követő egy napon belül jelentettek. Az esemény során ultrahangos vezérlésű kompresszióra és a pszeudoaneurizmába történő trombin befecskendezésére volt szükség, ami tovább hosszabbította a beteg kórházi kezelését.

A vizsgálat 1. részében jelentett 5 nemkívánatos esemény közül 1 valószínűleg az eszközzel kapcsolatos nemkívánatos esemény volt: a beavatkozást követő 1 napon élénk rövid ideig tartó vérzés nem súlyos eseménye. A vizsgálat 2. részében jelentett 19 nemkívánatos esemény közül 3, az eszközzel kapcsolatos, nem-súlyos, hematómával kapcsolatos nemkívánatos eseményt figyeltek meg, valamint 6, az eszközzel kapcsolatos, nem-súlyos eseményt figyeltek meg, beleértve 3 tartós nedvszivárgást, 2 hematómát és 1 testmozgást követő lábfájdalmat.

A 2. részben 3 betegnél értékelték kezelési kudacként a beavatkozást: 2 esetben kompresszió nélkül a vérzéscsillapítás elégtelensége miatt, és 1 esetben súlyos érrendszeri szövődmény (pszeudoaneurizma) miatt. A vizsgálat 1. részében nem fordult elő kezelési kudarc.

A vizsgálat 2. részének hat eszközhibája közül három nem akadályozta az eljárást, az egyik a felhasználói hibára, egy a bevezető szivárgására, egy pedig elszakadt szálizületre vezethető vissza. Az utolsó két problémát a C11202-ben megvalósított modellfrissítésekkel oldottuk meg.

A forgalomba hozatal előtti klinikai vizsgálat 2. része nem jelentett 6 hónapos utánkövetési eredményeket a betegek együttműködésének hiánya miatt. A forgalomba hozatal előtti klinikai vizsgálat (EU-SE-001) 30 napos eredményei, amelyek összhangban vannak a klinikai irodalomban leírt utánkövetési időszakokkal, azt mutatják, hogy a FemoSeal™ VCS biztonságos és hatásos.

## 1.4.2 A forgalomba hozatalt követő klinikai vizsgálatok adatainak összefoglalása

Az alábbi, **1.6 táblázatban** 4 elvégzett, forgalomba hozatal utáni klinikai vizsgálat szerepel. Ezek a klinikai vizsgálat kerültek publikálásra és nem érhetők el online.

**1.6 táblázat: Forgalomba hozatal utáni klinikai vizsgálatok**

| Elvégzett, forgalomba hozatal utáni klinikai vizsgálatok                                    |              |                                                                                |                                                                                                                                                                                                                                                 |                                                                                                                                                                             |                                                                                                                                                             |
|---------------------------------------------------------------------------------------------|--------------|--------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Vizsgálat neve                                                                              | Év / CI      | Vizsgálat típusa                                                               | Célkitűzések                                                                                                                                                                                                                                    | Mérföldkövek                                                                                                                                                                | Lehetséges elfogadási kritériumok                                                                                                                           |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI | A forgalomba hozatal utáni klinikai vizsgálat, az új csomagolások felhasználói | A forgalomba hozatal utáni vizsgálatban a FemoSeal Vascular® zárórendszer #11202-es modellfrissítését végezték el, amely módosított szállítórendszerrel rendelkezik az első, #11200-as modellhez képest, hogy dokumentálja a funkcionálisitást. | 100 beteg <ul style="list-style-type: none"> <li>63 férfi / 37 nő</li> <li>Átlag életkor 68 év nőknek, 65 év férfiaknak</li> </ul> 2 svéd kórház, 6 orvos<br><br>112 eszköz | Eredmények<br><br>1.A használati útmutatóban található ábrák/utasítások tájékoztató jellegűek és elégségesek.<br><br>2. Azonnali vérzéscsillapítás (91/100) |

|                                                                                   |                                                            |                                               |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-----------------------------------------------------------------------------------|------------------------------------------------------------|-----------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|----|-----|----------|-------|----------|-----------|----|----------|-----------|-------------------------|----------|--------------------|------------|---------------------|-----------|-------------------|---------|-----------------------|----------|--------------------------------|----------|----------------------|-----------|--------------------------|-----------|-----------------------------------|----------|----------------------|--------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                   |                                                            | elfogadhatósága                               | A vizsgálat célja az volt, hogy visszajelzést kapjon az átdolgozott használati útmutatóról (IFU), az orvosoknak és az ápolóknak szóló képzési projektről, megerősítse a kockázatelemzés során végzett értékeléseket, és visszajelzést adjon a termékminőség javításairól. | A betegnyilvántartási űrlapokon (CRF) rögzített adatok<br><br>Tervezett megfigyelési idő – 30 perc az alkalmazás időpontjától számítva                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008) | Dr. Nicolas Moes<br>Innsbruck Medical University, Ausztria | forgalomba hozatal utáni megerősítő értékelés | A vizsgálat célja a normál klinikai rutin során használt FemoSeal® biztonságosságának és teljesítményének felmérése volt 7F-hüvelyes diagnosztikai szívkatéterezési vagy perkután kardiális intervenciók beavatkozásán áteső betegeknél.                                  | 50 egymást követő beteg<br><br>Indikáció – diagnosztikus vagy invazív szívkatéterezés a közös combartériából<br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yr)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yr) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Elsődleges végpontok: <ul style="list-style-type: none"><li>Elsődleges hatásossági végpont – TTH (a vérzéscsillapításig eltelt idő) nedvszívárgással vagy anélkül, de bármilyen további, kézi vagy mechanikus kompressziós beavatkozás nélkül.</li><li>Biztonsági végpont – a nemkívánatos események előfordulása - kisebb és nagyobb vaszkuláris szövődmények és minden egyéb nemkívánatos esemény - súlyos és nem súlyos a vizsgálat időtartama alatt (azaz a beteg elbocsátásáig).</li></ul> Eredmények <ul style="list-style-type: none"><li>A vérzéscsillapításig eltelt átlagos idő</li><li>Diagnózis – 56,6 ± 29 másodperc</li><li>Beavatkozás 59,9 ± 16,2 másodperc</li><li>Minden beteg 57,8 ±26,3</li><li>Az összes beteg 4 órák ágyynyugalom után problémák nélkül ambulálható volt.</li></ul> Biztonságossági eredmények <ul style="list-style-type: none"><li>49/50 (98%) érrendszeri komplikációktól mentes a kórházi elbocsátásig</li><li>Átlagos ambulációs idő 2,6 nap</li><li>1/50 (2%) enyhe vérzés a következő napon egyenletlen vérellátás után angiográfia napján</li></ul> |
| n                                                                                 | 50                                                         |                                               |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| men                                                                               | 35 (70%)                                                   |                                               |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| women                                                                             | 15 (30%)                                                   |                                               |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| PCI cases                                                                         | 15                                                         |                                               |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| age (yr)                                                                          | 62.8±11.1                                                  |                                               |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| body mass index (kg/m²)                                                           | 25.4±6.7                                                   |                                               |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| systolic BP (mmHg)                                                                | 131.2±20.9                                                 |                                               |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| diastolic BP (mmHg)                                                               | 77.9±10.6                                                  |                                               |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| diabetes mellitus                                                                 | 9 (18%)                                                    |                                               |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| arterial hypertension                                                             | 34 (68%)                                                   |                                               |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| previous coronary intervention                                                    | 13 (26%)                                                   |                                               |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| preprocedure aspirin                                                              | 50 (100%)                                                  |                                               |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| preprocedure clopidogrel                                                          | 50 (100%)                                                  |                                               |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Procedural unfractionated heparin                                                 | 15 (30%)                                                   |                                               |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Procedural abciximab                                                              | 2 (4%)                                                     |                                               |                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |   |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |

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| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | 2009 RADI                       | Forgalomba hozatal utáni vizsgálat                                           | <p>A vizsgálat során tájékoztatni kell a beteget/felhasználót, ha bármilyen problémát észlel az új csomagolással, különösen a Tuvek/PET-PE tasak nem steril külső oldalával kapcsolatban.</p> <p>A vizsgálatnak arról is tájékoztatnia kell a kezelőorvost, hogy az eszköz alkalmazásában/behelyezéseben bármilyen különbség mutatkozik-e a korábban használt eszközökhöz képest.</p> <p>A vizsgálatnak a termékminőség esetleges további javítására is javaslatokkal kell szolgálnia.</p> | <p>25 eszköz</p> <p>4 svéd kórház</p> <p>A betegek 16/25-e (64%-a) PCI-(perkután-coronaintervenció)-beteg volt, akik erős véralvadást gátló gyógyszereket szedtek</p>                                                                                                                                                                                                                                                                                          | <p>Eredmények</p> <ol style="list-style-type: none"> <li>Csomagolással kapcsolatos problémák – 21/25 (84%) sikeres alkalmazás volt; 4/25 (16%) sikertelen volt (1 - új behelyező tesztelése, 1 belső korong, ha az arteriotómián keresztül a támogató lépésben a gomb feljött, és a külső korong a bemetszési szövetsatornába lett behelyezve, 2 azonnali vérzéscsillapítást nem sikerült elérni a behelyezési problémák hiánya ellenére sem.)</li> <li>Azonnali vérzéscsillapítás 19/25 (76%) betegeknél</li> <li>Vérzés 11/25 (44%) - 9/25 (36%) nedvszivárgás/vérzés, 2/25 (8%) hematoma</li> </ol> <p>Teljes eseményráta 19%</p>                                                                                                                                                           |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022) | 2022/Terumo Medical Corporation | Prospektív, többközpontú, forgalomba hozatal követő megfigyelés és vizsgálat | <p>A vizsgálat célja a FemoSeal™ VCS biztonságosságának és hatásosságának további bizonyítása a közös combartéria (CFA) hozzáférési helyeken végzett vérzéscsillapítás elérése során a perkután endovaszkuláris eljárásokon áteső valós alanyok esetében</p>                                                                                                                                                                                                                               | <ul style="list-style-type: none"> <li>A betegek utánkövetése 30. napon (<math>\pm 7</math> nap) kórházi látogatással vagy telefonhívással.</li> <li>Bevonás: 2021 decembertől 2022 júliusig.</li> <li>A tervek szerint: 230 diagnosztikai vagy intervenció endovaszkuláris eljárásokon áteső bevont alany, akiknél FemoSeal™-t használnak</li> </ul> <p>3 európai vizsgálati hely: Franciaország (92 beteg), Németország (38 beteg), Belgium (100 beteg).</p> | <ul style="list-style-type: none"> <li><b>Demográfiai adatok/társbetegségek:</b> <ul style="list-style-type: none"> <li>Nem: 161 férfi (70%) / 69 nő 69 (30%).</li> <li>Átlagéletkor: <math>70 \pm 12</math>.</li> <li>BMI: <math>26,1 \pm 4,95</math> kg/m<sup>2</sup>.</li> <li>Magas vérnyomás: 160 beteg (69,6%).</li> <li>Dyslipidemia: 128 (55,7%).</li> <li>Koronáriabetegség: 42 (18,3%).</li> <li>Jelenlegi dohányos: 86 (37,6 %).</li> <li>Korábbi dohányos: 66 (28,8%).</li> <li>Szívkoszorúér-betegség 34 (14%).</li> <li>Szívizominfarktus előzménye 18 (7,8%).</li> <li>Perifériás artériás revascularizáció: 12 (5,2%) carotis és 83 (37,5%) és alsó végtag artéria.</li> <li>Trombocitaaggregáció-gátló terápia (a kiindulási állapotban): 211 (91,7%),</li> </ul> </li> </ul> |

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|  |  |  |  |  | <p>beleértve 21 (9,1%)<br/>kettős<br/>trombocitaaggregáció-<br/>gátló terápiát (DAPT).</p> <p>- Orális véralvadásgátlás:<br/>40 (17,4%) beteg.</p> <p>• <b>Beavatkozási jellemzők:</b></p> <p>- Beállítás: fekvőbeteg<br/>klinika 162 eset (70,4%),<br/>ambuláns klinika 68 eset<br/>(29,6%).</p> <p>- Elsődleges indikáció:<br/>klaudikáció 147 eset<br/>(63,9%).</p> <p>- Megközelítés: 35<br/>antegrád (15,3%), 194<br/>retrográd (84,7%).</p> <p>• <b>Elsődleges végpontok:</b></p> <p>- Kombinált<br/>biztonságosság (a<br/>hozzáférési helyen a<br/>végtag súlyos<br/>szövődményeitől való<br/>mentesség az eljárást<br/>követő 6 órán belül) és<br/>hatásosság (sikeres<br/>vérzéscsillapítás a<br/>punkció helyén) végpont<br/>215/226-ban (95,1%)<br/>[95%-os CI: 91,46;<br/>97,55] beteg a teljes<br/>elemzési készletben és<br/>215/230 (93,5%) [95%-os<br/>CI 89,47, 96,30] a<br/>FemoSeal™-l kezel<br/>készletben.</p> <p>- A hatásossági végpontot<br/>219/226 (96,9%) CI<br/>[93,7, 98,7] betegnél<br/>érték el.</p> <p>- A biztonságossági<br/>végpontot 220/230<br/>(95,2%) [95%-os CI:<br/>92,15, 97,90] betegnél<br/>érték el.</p> <p>• <b>Másodlagos végpontok:</b></p> <p>- A beavatkozást követő<br/>hat órán belül 225/230<br/>(97,8%) betegnél sikerült<br/>megszüntetni a<br/>hozzáférési helyen</p> |
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|  |  |  |  |  | <p>jelentkező kisebb szövődményeket [95%-os CI: 95,00; 99,29].</p> <p>- 219/230 (95,2%) [95%-os CI: 91,60; 97,59] beteg esetében a beavatkozást követő hat órától a 30. napig nem jelentkeztek súlyos és kisebb szövődmények a hozzáférési helyen.</p> <p>- A FemoSeal™ VCD-szal elért vérezscsillapítás átlagos ideje: 0,42 (0,25; 0,50) perc.</p> <p>- Ambulációig eltel átlagos idő: 5,00 (4,54; 5,50) perc.</p> <p>- Kórházi tartózkodás átlagos időtartama: 23,98 (22,72, 25,00) óra.</p> <p>- A FemoSeal™ VCS használhatósága: az esetek 98,7%-ában „könnyen” vagy „nagyon könnyen” telepíthető (21 esetben „könnyen” (9,2%), 205 esetben „nagyon könnyen” telepíthető (89,5%), 226 esetben (98,3%) nem volt ellenállás vagy csak csekély ellenállás volt tapasztalható a behelyezéskor.</p> <p>A FemoSeal™ készletben (GW 0.038") található és a FemoSeal™-ben ajánlott vezetődróttal kezelt betegek 152/230-ánál (66,1%) nem jelentettek semmilyen eszközhibát vagy mellékhatást.</p> |
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A 2006-os vizsgálatot azért végezték, hogy megerősítsék a jelenlegi eszköz biztonságát és hatásosságát egy továbbfejlesztett bejuttató rendszerrel, valamint visszajelzést kapjanak a FemoSeal™ VCS használati utasításáról és a képzési programról. A vizsgálatba 100 beteget vontak be, és az elsődleges végpont az volt, hogy elértek-e vérzéscsillapítást, vagy szükség volt-e további manuális vagy mechanikus kompressziókra. Ez a vizsgálat arra a következtetésre jutott, hogy a FemoSeal™ VCS alkalmazása az esetek többségében sikeres volt (91%-ban azonnali vérzéscsillapítást ért el).

A 2008-as vizsgálatba 50 beteget vontak be a FemoSeal™ VCS biztonságosságának és teljesítőképességének felmérésére a 7 Fr-es hüvellyel rendelkező szívkátéterezésein áteső betegeknél szokásos klinikai rutin eljárás során használata során. A vizsgálat elsődleges végpontja az volt, hogy adatokat gyűjtsenek a vérzéscsillapításhoz szükséges időre, valamint az ambulációig eltelt idő további, manuális vagy mechanikus kompresszió nélküli. A vizsgálat eredménye szerint a vérzéscsillapítás átlagos ideje 57,8 másodperc volt, és minden beteg 4 óra elteltével ambulálható volt.

A 2009-es vizsgálat szerint értékelték az új FemoSeal™ VCS csomagolást. A vizsgálatba 25 beteget vontak be. Az elsődleges végpont az volt, hogy a felhasználó tapasztalt-e bármilyen problémát a csomagolással kapcsolatban. A felhasználók nem észleltek problémát az új FemoSeal™ VCS csomagolással kapcsolatban. Ez a vizsgálat a vérzéscsillapításig eltelt időre vonatkozóan is gyűjtött adatokat.

A vizsgálat célja a FemoSeal VCS biztonságosságának és hatásosságának további bizonyítása a közös combartéria (CFA) hozzáférési helyeken végzett vérzéscsillapítás elérése során a perkután endovaszkuláris eljárásokon áteső valós alanyok esetében. A vizsgálatba 230 beteget vontak be. A nyilvántartás elsődleges végpontjai a beavatkozás sikeressége (azaz sikeres punkció a vérzés miatt), valamint a súlyos szövődmények (pl. érsérülés, a behatolási hellyel kapcsolatos vérzés, a behatolási hely fertőzése, ismételt manuális kompresszió és új, műtéti helyekkel kapcsolatos ipsilaterális akut lábi ischaemia) csökkenése. A vizsgálat arra a következtetésre jutott, hogy a FemoSeal™ VCS jól teljesít valós körülmények között, és hatékony vérzéscsillapítást és alacsony hozzáférési helyi szövődményarányt biztosít a perifériás endovaszkuláris beavatkozásokon áteső betegek számára. Jó teljesítményt mutat rövid vérzéscsillapítási idővel és jó kezelői visszajelzéssel, ami a FemoSeal™ VCS-t értékes eszközzé teszi a femorális hozzáférés lezárásához.

### **1.4.3 A forgalomba hozatalt követő klinikai vizsgálatok adatainak összefoglalása**

#### **1.4.3.1 Elvégzett, forgalomba hozatal utáni nyomonkövetés**

Az elvégzett forgalomba hozatalt követő klinikai utánkövetési tevékenységek összefoglalása az alábbi **1.7 táblázatban** található.

### 1.7 táblázat: Forgalomba hozatal utáni klinikai utánpótlási tevékenységek

| Elvégzett, forgalomba hozatal utáni klinikai utánpótlási tevékenységek    |           |                                                                       |                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|---------------------------------------------------------------------------|-----------|-----------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Tevékenység neve                                                          | Év/CI     | Vizsgálat típusa                                                      | Célkitűzések                                                                                                                                                                                                                                                                                                                                              | Mérföldkövek                                                                                                                                                                                                                                                                                                                           | Lehetséges elfogadási kritériumok                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021 TMC  | Forgalomba hozatal utáni klinikai felmérés - kiváló minőségű felmérés | Forgalomba hozatalt követő felmérés az Európai Unió piacain forgalmazott FemoSeal™ Vascular Closure Device használatával kapcsolatos prospektív visszajelzések összegyűjtésére.                                                                                                                                                                           | <ul style="list-style-type: none"> <li>120 eset</li> <li>8 egyedi orvos, akik &gt; 5 éves tapasztalattal rendelkeznek</li> <li>Több ország Európában</li> </ul>                                                                                                                                                                        | <b>1–5 Skálájú Eszközürtékelés – Kérdőív állítások</b> <ul style="list-style-type: none"> <li>Elfogadási kritériumok <ul style="list-style-type: none"> <li>A 3–5-ös értékelés kedvezőnek minősül</li> <li>Minden állításnak ≥ 80%-ban pozitív visszajelzést kell kapnia</li> </ul> </li> <li>Eredmények <ul style="list-style-type: none"> <li>Nem érkezett válasz a felmérésre &gt; 20% kedvezőtlen válasz érkezett</li> <li>Nem érkezett panasz a termékkel kapcsolatban</li> </ul> </li> </ul> |
| 20210298 – 0,035” and 0038” Guidewire Clinical Survey Report (2021)       | 2021 TMC  | Forgalomba hozatal utáni klinikai felmérés - kiváló minőségű felmérés | Forgalomba hozatalt követő felmérés az Európai Unió piacain forgalmazott 6Fr Angio-Seal™ VIP Vascular Closure Device (VCD) eszközhöz mellékelt 0,035"-os vezetődrót, valamint a 8Fr Angio-Seal™ VIP VCD és FemoSeal Vascular Closure System eszközhöz mellékelt 0,038"-os vezetődrót használatával kapcsolatos prospektív visszajelzések összegyűjtésére. | <ul style="list-style-type: none"> <li>Felmérések 0,035"-ös vezetődróthoz <ul style="list-style-type: none"> <li>106 felmérés</li> <li>64 orvos</li> </ul> </li> <li>Felmérések 0,038"-as vezetődróthoz <ul style="list-style-type: none"> <li>109 felmérés</li> <li>55 orvos</li> </ul> </li> <li>12 retrospektív felmérés</li> </ul> | <b>1–5 Skálájú Eszközürtékelés – Kérdőív állítások</b> <ul style="list-style-type: none"> <li>Elfogadási kritériumok <ul style="list-style-type: none"> <li>A 3–5-ös értékelés kedvezőnek minősül</li> <li>Minden állításnak ≥ 80%-ban pozitív visszajelzést kell kapnia</li> </ul> </li> <li>Eredmények <ul style="list-style-type: none"> <li>Minden vezetődrót elfogadható minősítést kapott</li> <li>Nem érkezett panasz a termékkel kapcsolatban</li> </ul> </li> </ul>                       |
| FemoSeal™ Vascular Closure System                                         | 2023-2024 | Forgalomba hozatal utáni klinikai                                     | Az EU piacán forgalmazott FemoSeal VCS vezetődróttal való                                                                                                                                                                                                                                                                                                 | <ul style="list-style-type: none"> <li>126 felmérés</li> <li>7 felmérés hely</li> <li>5 országban</li> </ul>                                                                                                                                                                                                                           | <b>5 Skálájú Eszközürtékelés – Kérdőív állítások</b> <ul style="list-style-type: none"> <li>Elfogadási kritériumok</li> </ul>                                                                                                                                                                                                                                                                                                                                                                      |

| Elvégzett, forgalomba hozatal utáni klinikai utánpótlási tevékenységek                                                        |            |                                              |                                                                              |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|-------------------------------------------------------------------------------------------------------------------------------|------------|----------------------------------------------|------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PMCF<br>Clinical<br>Survey<br>Report:<br>Addressing<br>Gaps<br>Identified in<br>CER-FS-<br>2021 and<br>CER-FS-<br>2022 (2023) | TMC/<br>TE | felmérés -<br>kiváló<br>minőségű<br>felmérés | használatával<br>kapcsolatos<br>visszajelzések<br>prospektív<br>gyűjtéséhez. | <ul style="list-style-type: none"> <li>2023. november 14. -<br/>2024. június 11.</li> <li>Orvos szakterülete: <ul style="list-style-type: none"> <li>Érrendszeri<br/>sebész</li> <li>Intervenció<br/>radiológus</li> <li>Angiológus</li> </ul> </li> </ul> | <ul style="list-style-type: none"> <li>A 3–5-ös értékelés<br/>kedvezőnek minősül</li> <li>Minden állításnak <math>\geq</math><br/>80%-ban pozitív<br/>visszajelzést kell<br/>kapnia</li> <li>Ha a felmérés során<br/>nemkívánatos<br/>események<br/>jelentkeznek, akkor<br/>ezeknek a<br/>kockázatkezelés által<br/>várhatónak kell<br/>lenniük.</li> <li><u>Beteg demográfia:</u> <ul style="list-style-type: none"> <li>Nő: 29,4% (37/126)</li> <li>Férfi: 69,8%<br/>(88/126)</li> <li>Nemi identitás: 0,8<br/>(1/126)</li> <li>Életkor &gt;75 év:<br/>31,7%</li> </ul> </li> <li>Eredmények <ul style="list-style-type: none"> <li>A FemoSeal™ VCS-<br/>hez mellékelt<br/>vezetődrót: 101/126<br/>(80,2%).</li> <li>Eljárás időtartama<br/>(perc): 63,4 (36,6)<br/>(átlag (SD)); 57,0<br/>(36,0-81,0)<br/>(középérték (IQR))</li> <li>Minden FemoSeal™<br/>VCS<br/>teljesítményértékelés<br/>kedvező volt.</li> <li>A FemoSeal™ VCS<br/>által biztosított<br/>összes vezetődrót<br/>értékelése kedvező<br/>volt.</li> <li>Egy (0,8%)<br/>nemkívánatos<br/>esemény: a<br/>FemoSeal™ VCS<br/>korongok helyzete</li> </ul> </li> </ul> |



| Elvégzett, forgalomba hozatal utáni klinikai utámkövetési tevékenységek |  |  |  |  |                                                                                                                                                                                                              |
|-------------------------------------------------------------------------|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                         |  |  |  |  | valószínűleg nem volt megfelelő, mert olyan merev vezetődrtöt használtak (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 hüvelyk), amely manuális kompressziót igényelt a vérzéscsillapítás eléréséhez. |

A Terumo Medical Corporation három magas színvonalú orvosfelhasználói felmérést végzett a jelenlegi jelentési időszakban (2019. szeptember 1. – 2024. augusztus 31.).

A FemoSeal™ klinikai vizsgálatok proaktív klinikai adatokat gyűjtöttek a FemoSeal™ VCS biztonságosságával és teljesítményével kapcsolatban a klinikai használat során. A felmérésben olyan kérdések merültek fel, amelyek a teljes eszközre és a kapcsolódó tartozékokra összpontosítottak, beleértve a 0,038"-os vezetődrtöt és közvetlen interakcióikat. A Guidewire klinikai vizsgálatok a FemoSeal™ VCS-hez mellékelt 0,038"-os vezetődrt klinikai használata során a biztonságosságra és a teljesítményre vonatkozóan proaktív klinikai adatokat gyűjtöttek. A felmérés a vezetődrt általános használatára összpontosított, a behelyezéstől az bevezetőhüvelyen át az érrendszerbe történő bevezetésig és a drót eltávolításáig.

Az eszökhöz mellékelt FemoSeal™ VCS és 0,038" vezetődrt megkapta az összes elfogadható minősítést és hat (6) panaszt az eszközre vonatkozóan, valamint kilenc (9) nem panasz-jellegű bejelentés a vezetődrtre vonatkozóan a kiváló minőségű klinikai vizsgálatokból származó megjegyzések értékelése alapján. A panaszokat mind a FemoSeal, mind a vezetődrt tekintetében értékelték, és a Terumo forgalomba hozatal utáni felügyeleti folyamatának részeként értékelték. Nem azonosítottak új kockázatokat és kockázati szinteket.

A PMCF-tevékenységek keretében 2024-ben orvosi felhasználói felmérést végeztek. A felmérés eredményei azt mutatták, hogy a FemoSeal™ VCS teljesítményértékelése és biztonságossága általánosságban nagyon kedvező volt. A FemoSeal™ VCS-hez a mellékelt szabványos vezetődrttől eltérő más vezetődrtök kompatibilitását is bizonyították.

#### **1.4.3.2 Folyamatban lévő vagy tervezett, forgalomba hozatalt követő klinikai utánpótlás**

A TMC egy folyamatos/tervezett forgalomba hozatal utáni klinikai utánpótlási tevékenységet folytat. Sor kerül egy klinikai felmérésre, amely a vezetődrótnak az EU piacán forgalmazott FemoSeal VCS rendszer használatával kapcsolatos visszajelzések gyűjti össze utólagosan. A vizsgálatot az orvosok végzik el annak vizsgálatára, hogy milyen vezetődrótokat használtak a beavatkozás során. A kérdőív célja egy olyan hiányosság kezelése, amely a FemoSeal™ VCS-nek más, nem Terumo gyártmányú vezetődrótokkal való kompatibilitásáról szóló szakirodalom és külső szakértői vélemények hiányából adódik. A visszajelzés magában foglalja a technikai eredményeket, a klinikai teljesítményt és az eszköz különböző vezetődrótokkal való teljesítőképességére vonatkozó biztonságosságot.

#### **1.4.4 A szisztematikus szakirodalmi áttekintésből származó adatok összefoglalása**

A Terumo Medical Corporation szisztematikus szakirodalmi felülvizsgálatot végez a FemoSeal™ VCS és/vagy a hasonló eszközökkel kapcsolatban közzétett vizsgálatokból származó klinikai biztonságossági és teljesítményadatok összegyűjtésére és értékelésére. A publikált szakirodalom éves szűrésének célja a korábban ismeretlen mellékhatások azonosítása, az ismert mellékhatások nyomon követése, a veszélyes kockázatok azonosítása, valamint az FemoSeal™ VCS lehetséges szisztematikus helytelen használata vagy rendeltetéstől eltérő használata.

A legutóbbi szisztematikus szakirodalom-felülvizsgálat, amely 2019. szeptember 1-től 2024. augusztus 31-ig tartó időszakra terjedt ki, 29 publikált vizsgálatot azonosított, amelyek klinikai biztonságossági és teljesítményadatokat szolgáltatnak az FemoSeal™ VCS-mel kapcsolatban. Huszonhárom referencia publikáció számolt be a FemoSeal™ VCS rendeltetésnek megfelelő és kilenc a rendeltetésen kívüli használatáról. Összességében a FemoSeal™ VCS használatára vonatkozó vizsgálatok szakirodalmi felülvizsgálata egy olyan vizsgálat alatti populációt mutat be, amely az EU-ban lévő, perkután érkatéterezési eljárásos áteső betegek egy reprezentatív populációja. Ezen 23, a rendeltetésnek megfelelő használatról beszámoló szakirodalmi publikációt lásd a **3. szakaszban**.

A klinikai teljesítőképességet a következő mérőszámok alapján értékelték:

- A vérzéscsillapításhoz szükséges idő jobb vagy hasonló a perkután végzett közös combaréria elzárás legkorszerűbb módszerével elért időhöz.
- Az ambulációhoz szükséges idő jobb, jobb vagy hasonló a perkután végzett közös combaréria elzárás legkorszerűbb módszerével elért ambulációs idő.
- A posztoperatív szövődmények aránya hasonló vagy alacsonyabb mint a jelenlegi standard kezelésnél megfigyelték.

Ezen klinikai teljesítőképesség mérések alapján a szakirodalomban szereplő adatok azt mutatták, hogy a FemoSeal™ VCS sikeresen használható a combartéria-punkció (arteriotomia) lezárására olyan betegeknél, akik 7 Fr vagy kisebb méretű bevezetőhüvelyt használva perkután katéterezéssel estek át. Az esetek többségében (79,65–100%) teljes vérzéscsillapítást értek el, és a vérzéscsillapításig eltelt átlagos idő 0,5 perc volt, az átlagos elbocsátási idő pedig 3 nap. A betegek 69,2–86,7%-a képes volt 5 órával a lezárás után járni, a műtét utáni átlagos fekvési idő 349 perc volt. A FemoSeal™ VCS elégtelenségét az esetek 3,68-4%-ában figyelték meg, és további manuális kompresszióra az eljárások 0,9–4,4%-ában volt szükség.

A klinikai biztonságosságot többek között az alábbi nemkívánatos események alapján értékelték:

- Vérzés
- Hematóma
- Pszeudoaneurizma
- Véraláfutás
- Arteriovenózus fisztula
- Fertőzés
- Halál

Az említett nemkívánatos események mindegyikénél a mellékelt vizsgálatokban a FemoSeal™ VCS alkalmazásával kapcsolatban jelentett előfordulási arány kisebb volt, vagy összevethető volt a manuális kompressziós és egyéb érlezáró eszközöknél tapasztalt arányokkal.

A 10 esettanulmány áttekintésével nem azonosítottunk nemkívánatos eseményt, mivel nem azonosítottunk új, nem várt, újonnan kialakuló vagy elfogadhatatlan kockázatokat.

A FemoSeal™ VCS diagnosztikai angiográfia vagy intervenciós műtét során történő használatának általános hatékonysága több tényezőtől függ, például: nemtől, életkortól, a beteg anatómiájától, társbetegségektől, a punkció helyének anatómiai elhelyezése, a sebész tapasztalata, a VCD behelyezési módszere, posztoperatív gondozás, stb. A technikai siker mellett, beleértve a vérzéscsillapítás elérését is, a FemoSeal™ VCS klinikai előnyöket kínált az érlezáráshoz képest a combartéria punkciója után, például a vérzéscsillapításig eltelt idő lerövidülését, az ambulációig eltelt idő lerövidülését. A FemoSeal™ VCS teljesítményeredményei megfelelnek az ilyen típusú eszközzel szembeni elvárásoknak, ha rendeltetésszerűen használják. A jelenlegi keresési időszak alatt lekért hivatkozások némelyike a szóban forgó eszközt a közös femorális artériától eltérő anatómiai helyen, valamint > 7 Fr arteriotómiák lezárására alkalmazta, ami nem indikáció szerinti alkalmazásnak minősül.

A felülvizsgálat során nem azonosítottak ismeretlen mellékhatásokat, felmerülő kockázatokat vagy az eszköz lehetséges szisztematikus helytelen használatát. Ha azonban a FemoSeal™ VCS-t képzett orvosok óvatosan használják, az orvostechnikai eszköz hasznos és szükséges klinikai

eszközként működik. Összességében a célterápia és így a FemoSeal™ VCS megfelel az érhozzáféréssel kapcsolatos szövödmények kezelésében jelenleg fennálló klinikai igényeknek.

Összességében a szakirodalomban szereplő adatok nem azonosítottak olyan teljesítmény- vagy biztonsági problémákat a klinikai környezetben, amelyek korábban ismeretlenek voltak, vagy a nemkívánatos hatások a várt/elfogadhatónál nagyobb arányban fordultak elő. Ezért ebből az irodalmi áttekintésből az a következtetés vonható le, hogy a FemoSeal™ VCS, ha a perkután katéterezést követően az arteriotómiában a hemosztázishoz kompresszió biztosítóra használják, továbbra is a várt módon működik, és nem jár komoly biztonsági eseményekkel.

#### **1.4.5 A forgalomba hozatalt követő klinikai vizsgálatok adatainak összefoglalása**

Megelőző PMS rendszer van érvényben, és minden panaszt havonta, a belső gyártási eljárásoknak megfelelően felülvizsgálunk. A reklamációs adatok elemzése a 2019. szeptember 1. és 2024. augusztus 31. közötti időszakokban történt. Összességében 28 orvosi eszköz figyelő (MDV) jelentés és 476 ügyfélpanasz-jelentés érkezett a gyártóhoz. A 28 MDV-jelentésből 27 nemkívánatos eseménnyel, egy pedig az eszköz meghibásodásával volt kapcsolatos. A jelentési időszak alatt két haláleset történt, de mindkét esetben úgy ítélték meg, hogy az esemény nem áll összefüggésben vizsgált eszközzel. A gyártónál benyújtott 476 panasz közül a leggyakoribb ok a bevezetési nehézségek voltak (146 előfordulás, 0,0142% előfordulási arány). A kihúzási események meghibásodási módja a második leggyakrabban előforduló, 0,0126%-os arányban (130 esemény).

A FemoSeal Vascular Closure System világszerte több mint 1 030 136, az Európai Gazdasági térségben pedig 827 843 értékesítést ért el. A panaszoknak a globális értékesítések alapján számított gyakorisága 0,046%. Az összesített ügyfélpanaszok aránya nagyon alacsony. Nem azonosítottak olyan új kockázatokat, amelyek nem szerepelnek a használati utasításban és a kockázati dokumentációban.

A mellékhatások előfordulási arányát az **1.2 táblázat** tartalmazza. A panaszok által nem azonosítottak új előre nem látható, felmerülő vagy elfogadhatatlan kockázatokat. Az ismert nemkívánatos mellékhatások gyakorisága vagy súlyossága nem emelkedett jelentősen.

#### **1.4.6 A klinikai teljesítmény és biztonság általános összefoglalása**

A FemoSeal™ VCS használata a közös combartéria-punkció (arteriotomia) lezárására javallt olyan betegeknél, akik 7F (2,33 mm) vagy kisebb bevezetőhüvely segítségével perkután katéterezésen estek át. Ez a klinikai értékelés a FemoSeal™ VCS rendeltetésszerű használatára vonatkozó, rendelkezésre álló forgalomba hozatal előtti és utáni klinikai adatok és szakirodalom átfogó elemzésén alapul.

A publikált szakirodalom átfogó áttekintését 2019. szeptember 1-től 2024. augusztus 31-ig végezték. A bizonyítékok 29, a FemoSeal™ VCS-re vonatkozó vizsgálatot foglaltak magukban.

A klinikai értékelés során rendelkezésre bocsátott bizonyítékok arra a következtetésre jutottak, hogy nevezett eszköz a javallatoknak megfelelően használva biztonságos és hatásos, és az eszközzel normál használati körülmények között összefüggő kockázatok vagy nemkívánatos mellékhatások elfogadható kockázatnak minősülnek a beteg számára nyújtott előnyökkel szemben. A nevezett eszközök teljesítményeredményei megfelelnek az ilyen típusú eszközzel szembeni elvárásoknak, ha rendeltetésszerűen használják.

A FemoSeal™ VCS használatával kapcsolatos lehetséges nemkívánatos mellékhatások közé tartoznak az arteriotómiás lezárás alternatív eszközeivel gyakran jelentett nemkívánatos események, például a vérzés és a hematóma. Összességében a FemoSeal™ VCS használatával kapcsolatosan jelentett nemkívánatos események előfordulási arányai megegyeznek a manuális kompressziós és hasonló érlezáró eszközökkel jelentett arányokkal. Pontosabban, a vérzés és a hematóma esetében a FemoSeal™ VCS esetében jelentett arányok alacsonyabbak, mint a hasonló érlezáró eszközök esetében jelentett arányok. A közölt irodalomból és a forgalomba hozatal utáni felügyeletből eredő minden egyes nemkívánatos eseményt előzőleg azonosítottak (lásd az **1.3 szakaszt**).

A klinikai biztonságosságra és teljesítményre vonatkozó meglévő adatok azt sugallják, hogy a beteg számára az érlezáró eszköz használata nyújtotta előnyök meghaladják a lehetséges kockázatokat, ha az eszközt a Használati utasításnak megfelelően használják.

Amint azt fentebb már említettük, a FemoSeal™ VCS-hez megadott adatok megmutatják, hogy a vizsgált eszközzel kapcsolatos adatok (pl. eszközhasználat, biztonságossági eredmények, klinikai teljesítmény és klinikai előnyök) konzisztensek az azonosított ekvivalens eszközök és a legkorszerűbb hasonló eszközökkel kapcsolatos adatokkal

A biztonsági adatok keresztelemzése nem talált hiányosságokat a következők között:

- A jelenlegi szakirodalomban említett adatok
- Az eszközre vonatkozó adatok kiértékelés alatt
- Az eszközre vonatkozó adat(ok) kiértékelés alatt
- A címkeszövegben és/vagy a használati utasításban említett adatok (vagyis a fennmaradó kockázatok, amelyeket a felhasználóval ismertetni kell).

A klinikai biztonságosságot a publikált klinikai szakirodalomban, a vállalat által szponzorált klinikai vizsgálatokban, a forgalomba hozatal utáni adatok áttekintésében azonosított szövődmények alacsony aránya, valamint a forgalomból való kivonások hiánya igazolja. A teljesítménnyel kapcsolatos aggályokat nem azonosították, az áttekintett szakirodalom tartalmazta a FemoSeal™ VCS a gyártó által meghatározott rendeltetésének megfelelő használatát.

## 1.5 Lehetséges diagnosztikai vagy terápiás alternatívák

Hagyományosan manuális kompresszió használatos a vérzéscsillapítás érkatéterezést követő elérésére az arteriotómiás területen. A manuális kompresszióhoz a beteg hosszú (az eljárás után legfeljebb 8 órán keresztül tartó) immobilizációja társul jelentős diszkomfortérzéssel és elhúzódó kórházi tartózkodással. Egy nemrégiben végzett szisztematikus felülvizsgálat megállapította, hogy a manuális kompresszióval végzett vérzéscsillapítás eléréséhez szükséges medián idő 20,8 perc.<sup>1</sup>

A manuális kompresszió alternatívái közé tartoznak a külső vérzéscsillapító eszközök, amelyek mechanikai kompressziót alkalmaznak az arteriotómiás területen. Ezek az eszközök nem rövidítik le a vérzéscsillapításhoz vagy az ambulációhoz szükséges időt, viszont a manuális kompresszió mechanikus kompresszióval történő helyettesítésével csökkentik a személyzettel szemben támasztott követelményeket. A mechanikus kompresszió alkalmazásával kapcsolatos nemkívánatos események arányai hasonlóak a manuális kompresszió esetében tapasztaltakhoz.

Az érlezáró eszközök, mint például a FemoSeal™ VCS, az arteriotómiás lezárására szolgálnak. Céljuk, hogy csökkentsék a vérzéscsillapításhoz szükséges időt, és lehetővé tegyék a korábbi ambulációt. A közelmúltban végzett szisztematikus felülvizsgálat, mely magában foglalta a 13 kereskedelmi forgalomban kapható eszköz értékelését, megállapította, hogy a vérzéscsillapítás érlezáró eszközzel történő eléréséhez szükséges medián idő 5,4 perc volt. Az egyes érlezáró eszközök medián vérzéscsillapítási ideje 1 perc (FemoSeal™ VCS) és 14 perc között volt; az eszközök többségének esetében 4–10 perc között.<sup>1</sup>

Az arteriotómiás terület lezárásával összefüggő, gyakran jelentett nemkívánatos események, manuális kompresszió, külső vérzéscsillapító eszközök és az érlezáró eszközök alkalmazásával, magukban foglalták a haematómát, a hozzáférési helyen fellépő vérzést, a pseudoaneurizmát, az arteriovenosus fistulát és a fertőzést. Ugyanez a szisztematikus felülvizsgálat (34 randomizált, kontrollált vizsgálat, 14 401 beteg) megállapította, hogy a nemkívánatos események aránya hasonló volt a manuális kompresszió és az érlezáró eszközök használata között, kivéve, hogy az érlezáró eszközök esetében erősebb vérzési tendenciák mutatkoztak.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Javasolt felhasználói profil és képzés

A FemoSeal™ Vascular Closure System tervezett felhasználói azok az orvosok, akik a közös combartérián keresztül képesek elvégezni az artériás hozzáférést és az endovaszkuláris eljárások lezárását, és részt vettek a Terumo Medical Corporation FemoSeal™ orvosoknak szóló oktatásán.



### 1.7 Vonatkozó harmonizált és általános szabványok

| Hivatkozási szabvány | Megfelelés/felülvizsgálat aktuális éve | Leírás                                                                                                                                   |
|----------------------|----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070            | 2014/AMD1:2018                         | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070         | 2014/A1:2018                           | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA guidance         | 2021. május 20.                        | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052           | 2015                                   | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213           | 2017                                   | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503           | 2020                                   | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182           | 2019                                   | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |
| EN ISO 13485         | 2016/A11:2021                          | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 13485            | 2016                                   | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 14644-1          | 2015                                   | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                  |
| EN ISO 14644-1       | 2015                                   | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                  |

| Hivatkozási szabvány     | Megfelelés/felülvizsgálat aktuális éve | Leírás                                                                                                                                                                   |
|--------------------------|----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14644-2              | 2015                                   | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2           | 2015                                   | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3              | 2019                                   | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3           | 2019                                   | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1              | 2003                                   | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1           | 2003                                   | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2              | 2003/TC1:2004                          | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| EN ISO 14698-2           | 2003/TC 1:2004                         | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| USP <788>                | Nem értelmezhető                       | PARTICULATE MATTER IN INJECTIONS                                                                                                                                         |
| EU Gyógyszerkönyv 2.9.19 | Nem értelmezhető                       | Particulate Contamination: Sub-Visible Particles                                                                                                                         |
| IEC 62366-1              | 2015                                   | Medical devices — Part 1: Application of usability engineering to medical devices                                                                                        |
| EN 62366-1               | 2015                                   | Medical devices — Part 1: Application of usability engineering to medical devices                                                                                        |



| Hivatkozási szabvány | Megfelelés/felülvizsgálat aktuális éve | Leírás                                                                                                               |
|----------------------|----------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| EN ISO 14971         | 2019/A11:2021                          | Medical devices — Application of risk management to Medical devices                                                  |
| ISO 14971            | 2019                                   | Medical devices — Application of risk management to Medical devices                                                  |
| ASTM F1980           | 2016                                   | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1       | 2020                                   | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1          | 2018                                   | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2       | 2006                                   | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2          | 2006                                   | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3       | 2014                                   | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3          | 2014                                   | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4       | 2017                                   | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4          | 2017                                   | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| EN ISO 10993-5       | 2009                                   | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| ISO 10993-5          | 2009                                   | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| EN ISO 10993-6       | 2016                                   | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |

| Hivatkozási szabvány | Megfelelés/felülvizsgálat aktuális éve | Leírás                                                                                                                                     |
|----------------------|----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-6          | 2016                                   | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| EN ISO 10993-10      | 2023                                   | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| ISO 10993-10         | 2021                                   | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| EN ISO 10993-11      | 2018                                   | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| ISO 10993-11         | 2017                                   | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| EN ISO 10993-12      | 2021                                   | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| ISO 10993-12         | 2021                                   | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| EN ISO 10993-17      | 2009                                   | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17         | 2002                                   | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18         | 2020/A1:2022                           | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |
| EN ISO 10993-18      | 2020/A1:2022                           | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |
| EN ISO 10993-23      | 2021                                   | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |
| ISO 10993-23         | 2021                                   | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |

| Hivatkozási szabvány | Megfelelés/felülvizsgálat aktuális éve | Leírás                                                                                                                                                                       |
|----------------------|----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F2382           | 2018                                   | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756            | 2017                                   | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>             | Nem értelmezhető                       | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>            | Nem értelmezhető                       | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72       | 2019                                   | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135         | 2014/A1:2019                           | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135            | 2014/A1:2018                           | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7       | 2008/A1:2022                           | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |
| ISO 10993-7          | 2008/A1:2019                           | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                                            |
| EN 556-1             | 2024                                   | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices              |
| EN ISO 11737-1       | 2018/A1:2021                           | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                                        |

| Hivatkozási szabvány | Megfelelés/felülvizsgálat aktuális éve | Leírás                                                                                                                                   |
|----------------------|----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11737-1          | 2018/A1:2021                           | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products    |
| EN ISO 11138-1       | 2017                                   | Sterilization of health care products - Biological indicators - Part 1: General requirements                                             |
| ISO 11138-1          | 2017                                   | Sterilization of health care products - Biological indicators - Part 1: General requirements                                             |
| EN ISO 11138-2       | 2017                                   | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| ISO 11138-2          | 2017                                   | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| EN ISO 15223-1       | 2016                                   | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| ISO 15223-1          | 2016                                   | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| EN 1041              | 2008/A1:2013                           | Information supplied by the manufacturer of medical devices                                                                              |
| EN ISO 11607-1       | 2020/A1:2023                           | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| ISO 11607-1          | 2019/A1:2023                           | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| EN ISO 11607-2       | 2020/A1:2023                           | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes       |

| Hivatkozási szabvány | Megfelelés/felülvizsgálat aktuális éve | Leírás                                                                                                                                                                     |
|----------------------|----------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11607-2          | 2019/A1:2023                           | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169           | 2016                                   | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M    | 2016                                   | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825           | 2018                                   | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096           | 2011 (R 2019)                          | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M-15     | 2015                                   | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24         | 2021                                   | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3          | 2020                                   | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |
| MDCG 2020-8          | 2020                                   | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                             |
| MDCG 2020-7          | 2020                                   | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                          |
| MDCG 2020-6          | 2020                                   | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                       |
| MDCG 2019-9 v1       | 2022                                   | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                   |

| Hivatkozási szabvány | Megfelelés/felülvizsgálat aktuális éve | Leírás                                                                                                                                                                                                                                                        |
|----------------------|----------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2019-8 v2       | 2020                                   | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15         | 2020                                   | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11         | 2021                                   | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19         | 2021                                   | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4       | 2021                                   | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2          | 2019                                   | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1          | 2019                                   | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7          | 2018                                   | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6          | 2018                                   | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |
| MDCG 2018-4          | 2018                                   | MDCG 2018-4 Annex: UDI database Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                                                                                                  |
| MDCG 2018-3 v1       | 2020                                   | Guidance on UDI for systems and procedure packs                                                                                                                                                                                                               |
| MDCG 2021-25         | 2021                                   | Regulation (EU) 2017/745 - application of MDR requirements to ‘legacy devices’ and to devices placed                                                                                                                                                          |

| Hivatkozási szabvány | Megfelelés/felülvizsgálat aktuális éve | Leírás                                                                                                                 |
|----------------------|----------------------------------------|------------------------------------------------------------------------------------------------------------------------|
|                      |                                        | on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC                               |
| Meddev 2.12-2 Rev 2  | 2012                                   | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2 |

## 2.0 IRODALOMJEGYZÉK

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### 3.0 FELÜLVIZSGÁLATI ELŐZMÉNYEK

| SSCP felülvizsgálat száma              | Kibocsátási dátum | Változás leírása                                                          | A bejelentett szervezet által hitelesített felülvizsgálat                                                                                                                                                                                                                                                                             |
|----------------------------------------|-------------------|---------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022                           | 2023. január 20.  | Első kiadás, MDR CE-tanúsítvány esetén                                    | <input checked="" type="checkbox"/> Igen<br>Validáció nyelve: English<br><input type="checkbox"/> Nem (csak IIa osztályú vagy néhány IIb osztályú beültethető eszközre vonatkozik (MDR, 52. cikk (4) szakasz 2. bekezdés), amelyek esetében az SSCP-t még nem validálta az NB)<br><input type="checkbox"/> Egyéb (kérjük, fejtse ki): |
| SSCP-AS-2023 – 1. átdolgozás           | 2024. március 15. | Frissítve a 2019. január 1-től 2023. december 31-ig tartó időszakra.      | <input checked="" type="checkbox"/> Igen<br>Validáció nyelve: English<br><input type="checkbox"/> Nem (csak IIa osztályú vagy néhány IIb osztályú beültethető eszközre vonatkozik (MDR, 52. cikk (4) szakasz 2. bekezdés), amelyek esetében az SSCP-t még nem validálta az NB)<br><input type="checkbox"/> Egyéb (kérjük, fejtse ki): |
| SSCP-FS-2024<br>1. Módosított változat |                   | Frissítve a 2019. szeptember 1-től 2024. augusztus 31-ig tartó időszakra. | <input type="checkbox"/> Igen<br>Validáció nyelve: English<br><input type="checkbox"/> Nem (csak IIa osztályú vagy néhány IIb osztályú beültethető eszközre vonatkozik (MDR, 52. cikk (4) szakasz 2. bekezdés), amelyek esetében az SSCP-t még nem validálta az NB)<br><input type="checkbox"/> Egyéb (kérjük, fejtse ki):            |

|                                        |               |                                                                    |                                                                                                                                                                                                                                                                                                                                                              |
|----------------------------------------|---------------|--------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>2. Módosított változat | June 20, 2025 | Az NSAI validálásra<br>vonatkozó lekérdezései<br>alapján módosítva | <input checked="" type="checkbox"/> Igen<br>Validáció nyelve: English<br><br><input type="checkbox"/> Nem (csak IIa osztályú vagy<br>néhány IIb osztályú beültethető<br>eszközre vonatkozik (MDR, 52.<br>cikk (4) szakasz 2. bekezdés),<br>amelyek esetében az SSCP-t<br>még nem validálta az NB)<br><br><input type="checkbox"/> Egyéb (kérjük, fejtse ki): |
|----------------------------------------|---------------|--------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

## Riepilogo delle prestazioni cliniche e di sicurezza

### FemoSeal™ Vascular Closure System

|                                                                       |                                                                                             |
|-----------------------------------------------------------------------|---------------------------------------------------------------------------------------------|
| <b>Fabbricante</b>                                                    | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 Stati Uniti |
| <b>SRN del fabbricante</b>                                            | US-MF-000019594                                                                             |
| <b>Rappresentante della<br/>direzione/PRRC</b>                        | Kimberly Feitl<br>Vice President, Quality                                                   |
| <b>Basic UDI-DI</b>                                                   | 38970FS79                                                                                   |
| <b>Numero EMDN</b>                                                    | C900199 - Sistemi per emostasi - Altro                                                      |
| <b>Classe del dispositivo</b>                                         | Classe III                                                                                  |
| <b>Anno in cui il dispositivo ha<br/>ottenuto il primo marchio CE</b> | 2005                                                                                        |
| <b>Rappresentante UE</b>                                              | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgio<br>SRN: BE-AR-000001433 |
| <b>Organismo notificato</b>                                           | NSAI<br>CE 0050                                                                             |

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Questo Riepilogo delle prestazioni cliniche e di sicurezza (SSCP) ha lo scopo di consentire al pubblico di accedere a un riepilogo aggiornato dei principali aspetti della sicurezza e delle prestazioni cliniche di FemoSeal™ Vascular Closure System (VCS).

Di seguito, nella **Sezione 1.0**, è riportato un riepilogo delle prestazioni cliniche e di sicurezza del dispositivo, destinato agli utenti/operatori sanitari.



## **1.0 RIEPILOGO PER UTENTI/OPERATORI SANITARI**

L'SSCP non intende sostituire le Istruzioni per l'uso, che rappresentano il documento principale per garantire un uso sicuro del dispositivo, né fornire agli utenti o ai pazienti suggerimenti diagnostici o terapeutici. L'SSCP non intende sostituire le informazioni obbligatorie riportate sulle schede di impianto o in qualsiasi altro documento obbligatorio.

### **1.1 Uso previsto del dispositivo**

#### **1.1.1 Uso previsto**

FemoSeal™ Vascular Closure System è un dispositivo medico indicato per la chiusura di una puntura arteriosa dopo cateterizzazione percutanea attraverso l'arteria femorale comune.

#### **1.1.2 Indicazioni d'uso**

FemoSeal™ Vascular Closure System è indicato per l'uso nella chiusura della puntura dell'arteria femorale comune (arteriotomia) in pazienti sottoposti a cateterizzazione percutanea con introduttore procedurale pari o inferiore a 2,33 mm (7 F).

#### **1.1.3 Controindicazioni e/o limitazioni**

FemoSeal™ Vascular Closure System è controindicato nei pazienti con arteriotomie in cui sono stati utilizzati introduttori o dispositivi più grandi di 2,33 mm (7 F).

#### **1.1.4 Categorie di pazienti target**

La sicurezza e l'efficacia di FemoSeal™ Vascular Closure System sono state stabilite in pazienti di età pari o superiore a 18 anni che sono stati sottoposti a cateterizzazione percutanea utilizzando un introduttore procedurale di dimensioni pari o inferiori a 2,33 mm (7F).

#### **1.1.5 Categorie specifiche di pazienti**

La sicurezza e l'efficacia di FemoSeal™ Vascular Closure System non sono state dimostrate nelle seguenti categorie di pazienti:

- Pazienti con malattia autoimmune preesistente.
- Pazienti sottoposti a trombolisi terapeutica.
- Pazienti con malattia vascolare periferica clinicamente significativa.
- Pazienti con ipertensione non controllata (> 220 mmHg sistolica o > 110 mmHg diastolica).
- Pazienti con disturbi della coagulazione, tra cui trombocitopenia (< 100.000 piastrine) o anemia (Hgb < 10 mg/dl).
- Pazienti con lume interno dell'arteria femorale comune inferiore a 5 mm.

- Pazienti con compromissione renale e/o epatica.
- Pazienti con altra comorbidità rilevante.
- Pazienti con origini razziali e/o etniche specifiche.
- Pazienti con infarto del miocardio entro 72 ore.
- Pazienti con innesto o stent vascolare nel sito di venipuntura.
- Pazienti in gravidanza o in allattamento.
- Pazienti di età inferiore a 18 anni.

### 1.1.6 Utilizzatori previsti

Gli utilizzatori previsti di FemoSeal™ Vascular Closure System sono medici con una formazione che li abilita a eseguire accessi e chiusure arteriose per procedure endovascolari attraverso l'arteria femorale comune e che hanno partecipato a un programma di formazione per medici FemoSeal™ di Terumo Medical Corporation.

## 1.2 Descrizione del dispositivo

### 1.2.1 Descrizione del dispositivo

FemoSeal™ Vascular Closure System, prodotto da Terumo Medical Corporation (TMC), è un dispositivo di chiusura vascolare riassorbibile progettato per ottenere l'emostasi dell'arteria femorale dopo la cateterizzazione percutanea attraverso l'arteria femorale comune.

Gli elementi di chiusura FemoSeal™ sono costituiti da due dischi polimerici riassorbibili, un disco sigillante interno e un disco di bloccaggio esterno, che sono tenuti insieme da un multifilamento riassorbibile, che chiude meccanicamente l'arteriotomia (vedere **Figura 1.1** e **Figura 1.2**). Dopo essere stato posizionato attraverso l'introduttore con alloggiamento a cono, il disco di bloccaggio esterno viene compresso sullo shaft multifilamento, con conseguente chiusura meccanica del sito di venipuntura tra il disco di bloccaggio interno e quello esterno. Il disco sigillante interno e il disco di bloccaggio esterno sono tenuti in posizione grazie all'attrito sullo shaft multifilamento. L'emostasi si ottiene con mezzi meccanici. Gli elementi di chiusura si degradano per idrolisi.

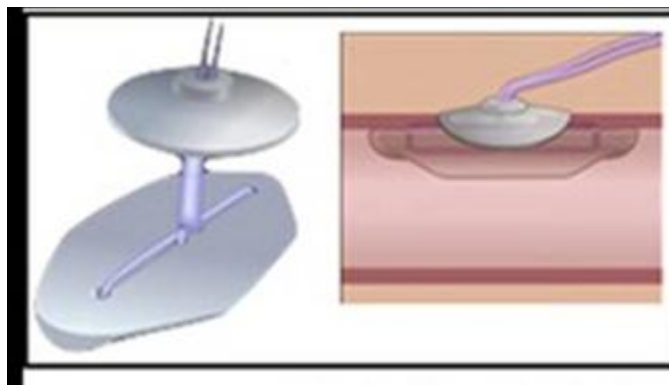
I componenti della chiusura impiantabile, il disco di sigillo interno e il disco di bloccaggio esterno, si degradano in diciotto (18) mesi, mentre si stima che il multifilamento si degradi e venga assorbito per idrolisi dai tessuti circostanti dopo due (2) o tre (3) anni. La capacità dei componenti di chiusura impiantabili di mantenere la compressione sull'arteriotomia è stata testata fino a otto (8) ore. I prodotti della degradazione vengono metabolizzati ed espulsi nell'urina o espirati come

anidride carbonica attraverso i polmoni. Negli studi sugli animali non sono stati osservati effetti da accumulo. I componenti aggiuntivi di FemoSeal™ che entreranno in contatto con tessuti viventi o sangue durante la procedura sono l'introduttore con alloggiamento a cono, il dilatatore, il tubo di compattazione, lo spintore e il filo guida.

**Figura 1.1 Disco sigillante interno e disco di bloccaggio esterno rispettivamente**

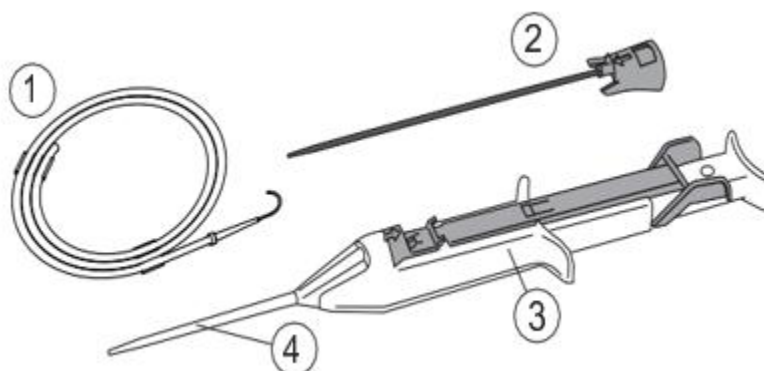


**Figura 1.2 Disco sigillante interno e disco di bloccaggio esterno posizionati**



L'unità FemoSeal™ è fornita insieme a un dilatatore e a un filo guida con diametro esterno di 0,97 mm (0,038") e lunghezza di 70 cm (27,5") e un raddrizzatore a J; vedere la **Figura 1.3** di seguito. È contenuto in un tubo di polietilene. Tutte le parti sono confezionate in un vassoio di carta fisso. La confezione include anche la scheda di impianto del paziente. FemoSeal™ Vascular Closure System non richiede accessori aggiuntivi per il funzionamento previsto del dispositivo, che deve essere utilizzato solo con il dilatatore e il filo guida inclusi nella confezione originale.

**Figura 1.3 Unità FemoSeal™ VCS con filo guida e dilatatore**



### 1.2.2 Materie prime e componenti

La **Tabella 1.1** riportata di seguito elenca i componenti di FemoSeal™ VCS.

**Tabella 1.1 Materie prime e componenti di FemoSeal™ VCS**

| Codice parte | Descrizione                                                         |                                                                           | Materiali                                                                                                                                                                              |
|--------------|---------------------------------------------------------------------|---------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1            | Filo guida da 0,97 mm (0,038") con raddrizzatore a J per filo guida |                                                                           | Filo guida: acciaio inossidabile 304<br><br>Raddrizzatore a J: polipropilene, pigmento viola<br><br>Clip: polietilene<br><br>Tubo: polietilene                                         |
| 2            | Dilatatore FemoSeal                                                 |                                                                           | Connettore: tetraidrofurano, pigmento blu, polibutilene tereftalato (PBT)<br><br>Tubo: polietilene ad alta densità (HDPE), pigmento nero<br><br>Lubrificante: Silicone Dow Corning 360 |
| 3/4          | Unità FemoSeal                                                      | RD7 sagomato - Disco sigillante interno e il disco di bloccaggio esterno* | Copolimero di glicolide, carbonato di trimetilene, ε-caprolattone e TMP: trimetilolpropano (iniziatore)                                                                                |
|              |                                                                     | Multifilamento *                                                          | Copolimero segmentato di L,L-lattide, carbonato di trimetilene, ε-caprolattone e 1,3 propanediolo (iniziatore)                                                                         |

|  |  |                                       |                                                                                        |
|--|--|---------------------------------------|----------------------------------------------------------------------------------------|
|  |  |                                       | Il rivestimento è realizzato con un copolimero di glicolide, ε-caprolattone e L-lisina |
|  |  | Tubo di compattazione                 | Polipropilene                                                                          |
|  |  | Spintore                              | Acciaio inossidabile 304V                                                              |
|  |  | Pressa                                | Polibutilene tereftalato (PBT)                                                         |
|  |  | Alloggiamento                         | Polibutilene tereftalato (PBT)                                                         |
|  |  | Pulsante                              | Polibutilene tereftalato (PBT)                                                         |
|  |  | Coperchio pulsante                    | Copolimero di poliossimetilene (POM)/poliacetale                                       |
|  |  | Manicotto                             | Polibutilene tereftalato (PBT)                                                         |
|  |  | Distanziale                           | Polibutilene tereftalato (PBT)                                                         |
|  |  | Cono                                  | Polipropilene                                                                          |
|  |  | Coperchio alloggiamento               | Polibutilene tereftalato (PBT)                                                         |
|  |  | Fermo di sicurezza                    | Polibutilene tereftalato (PBT), pigmento blu                                           |
|  |  | Coperchio manicotto                   | Polibutilene tereftalato (PBT)                                                         |
|  |  | Guarnizione tubo                      | Shore in silicone A 70                                                                 |
|  |  | Guarnizione alloggiamento             | Shore in silicone A 50                                                                 |
|  |  | Molla                                 | Acciaio inossidabile 302                                                               |
|  |  | Introduttore con alloggiamento a cono | Polipropilene<br>Silicone Dow Corning 360, esano                                       |

\* Parte impiantabile del dispositivo; i componenti impiantabili sono compatibili con la RM

FemoSeal™ VCS è sterilizzato con ossido di etilene (EtO) ed è un dispositivo medico monouso. È pertanto progettato in modo tale da non poter essere riutilizzato.

### **Modalità di azione**

FemoSeal™ VCS favorisce l'emostasi meccanica mediante il posizionamento di elementi di chiusura impiantabili all'interno e all'esterno dell'arteria femorale comune. Il meccanismo che previene l'emorragia è fornito dal sigillo interno che chiude il sito di venipuntura e dal disco di bloccaggio esterno che mantiene in posizione il sigillo interno.

### 1.2.3 Benefici clinici

FemoSeal™ VCS offre i seguenti benefici clinici rispetto alla chiusura vascolare dopo una puntura dell'arteria femorale comune:

- Riduzione del tempo di emostasi<sup>1</sup>
- Riduzione del tempo per la deambulazione<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

### 1.2.4 Generazioni o varianti precedenti

- La prima versione di FemoSeal™ VCS (n. 11200) è stata venduta sul mercato europeo nel 2005 e parte del 2006.
- L'attuale FemoSeal™ VCS (n. 11202), con un sistema di infusione migliorato, è sul mercato dal 28 marzo 2006.

### 1.2.5 Accessori destinati all'uso in combinazione con il dispositivo

L'unità FemoSeal™ è fornita insieme a un dilatatore, un filo guida con diametro esterno di 0,97 mm (0,038"), lunghezza di 70 cm (27,5") e un raddrizzatore a J. Il filo guida è un accessorio dell'unità FemoSeal™. Il raddrizzatore a J è un componente del filo guida, mentre il dilatatore è un componente dell'unità FemoSeal™. Il filo guida è l'unico accessorio considerato. È contenuto in un tubo di polietilene. Tutte le parti sono confezionate in un vassoio di carta fisso. La confezione include anche la scheda di impianto del paziente. FemoSeal™ Vascular Closure System non richiede accessori aggiuntivi per il funzionamento previsto del dispositivo, che deve essere utilizzato solo con il dilatatore e il filo guida inclusi nella confezione originale.

### 1.2.6 Altri dispositivi e prodotti destinati a essere utilizzati in combinazione con il dispositivo

FemoSeal™ VCS non richiede ulteriori dispositivi per funzionare come previsto.

## 1.3 Rischi e avvertenze

### 1.3.1 Rischi residui ed effetti indesiderati

Gli eventi avversi noti o prevedibili, i danni e le complicanze associati all'uso del FemoSeal™ VCS come risultato del rischio residuo sono elencati nella **Tabella 1.2**. Il tasso di occorrenza si basa sull'analisi della documentazione del rischio e viene calcolato sulla base dei dati di monitoraggio post-commercializzazione dal 1° settembre 2019 al 31 agosto 2024. Non vi sono

rischi residui sconosciuti per FemoSeal™ VCS e tutti i rischi applicabili sono stati affrontati attraverso le Istruzioni per l'uso e il processo di gestione del rischio.

**Tabella 1.2. Eventi avversi/complicanze dei FemoSeal**

| Danno                                             | Frequenza (%) | Fattori di mitigazione                                                                                                                                                                                                    |
|---------------------------------------------------|---------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Reazione allergica                                | 0,0000        | Le azioni e i piani per mitigare il più possibile il rischio sono stati affrontati mediante caratteristiche di progettazione del prodotto, linee guida di produzione, etichettatura del prodotto e formazione dei medici. |
| Aneurisma                                         | 0,0000        |                                                                                                                                                                                                                           |
| Fistola AV                                        | 0,0001        |                                                                                                                                                                                                                           |
| Perdita di sangue/emorragia                       | 0,0280        |                                                                                                                                                                                                                           |
| Decesso                                           | 0,0002        |                                                                                                                                                                                                                           |
| Ecchimosi                                         | 0,0000        |                                                                                                                                                                                                                           |
| Embolia                                           | 0,0000        |                                                                                                                                                                                                                           |
| Reazione al corpo estraneo                        | 0,0000        |                                                                                                                                                                                                                           |
| Ematoma                                           | 0,0027        |                                                                                                                                                                                                                           |
| Emorragia                                         | 0,0001        |                                                                                                                                                                                                                           |
| Infezione                                         | 0,0002        |                                                                                                                                                                                                                           |
| Reazione infiammatoria                            | 0,0000        |                                                                                                                                                                                                                           |
| Intorpidimento                                    | 0,0000        |                                                                                                                                                                                                                           |
| Dolore                                            | 0,0000        |                                                                                                                                                                                                                           |
| Malessere del paziente                            | 0,0004        |                                                                                                                                                                                                                           |
| Ritardo della procedura                           | 0,0065        |                                                                                                                                                                                                                           |
| Pseudoaneurisma                                   | 0,0004        |                                                                                                                                                                                                                           |
| Emorragia retroperitoneale                        | 0,0002        |                                                                                                                                                                                                                           |
| Sepsi                                             | 0,0000        |                                                                                                                                                                                                                           |
| Tromboembolia                                     | 0,0000        |                                                                                                                                                                                                                           |
| Trombosi                                          | 0,0001        |                                                                                                                                                                                                                           |
| Occlusione dei vasi/ischemia degli arti inferiori | 0,0002        |                                                                                                                                                                                                                           |
| Perforazione vascolare                            | 0,0000        |                                                                                                                                                                                                                           |
| Dissezione/lacerazione dei tessuti vascolari      | 0,0003        |                                                                                                                                                                                                                           |

### 1.3.2 Avvertenze e precauzioni

#### Avvertenze

1. Non utilizzare se la confezione è danneggiata o se la barriera sterile non è intatta.
2. Non utilizzare dopo la data di scadenza: le prestazioni dei componenti biodegradabili potrebbero essere insufficienti.
3. Non utilizzare in caso di elementi che appaiono danneggiati o difettosi.
4. L'uso di FemoSeal™ Vascular Closure System in caso di contaminazione batterica dell'introduttore procedurale o del tessuto circostante può causare infezioni.
5. Se si sospetta che la parete dell'arteria posteriore sia stata perforata o che sia stata eseguita più di una puntura arteriosa, non affidarsi esclusivamente a FemoSeal™ Vascular Closure System per ottenere l'emostasi arteriosa. Utilizzare una compressione manuale o meccanica aggiuntiva.
6. Se il sito di venipuntura si trova in corrispondenza o in posizione distale rispetto alla biforcazione dell'arteria femorale, non utilizzare FemoSeal™ Vascular Closure System a causa del rischio di posizionamento errato del sigillo interno. Questo evento può causare complicazioni emorragiche e/o l'interruzione della normale portata di sangue.
7. In caso di emorragia arteriosa persistente dal sito di incisione, non tagliare il multifilamento fino al raggiungimento dell'emostasi. Se non si ottiene l'emostasi, fissare il multifilamento con una medicazione sterile e applicare una compressione supplementare fino a raggiungerla. In caso di emorragia arteriosa persistente, possono verificarsi complicanze emorragiche significative che possono causare lesioni o decesso del paziente.
8. Non utilizzare FemoSeal™ Vascular Closure System se il sito di venipuntura è vicino al legamento inguinale, in quanto potrebbe verificarsi un ematoma retroperitoneale.
9. I soggetti ad alto rischio di emorragia possono soffrire di una maggiore perdita di sangue, che richiede una trasfusione.
10. Se il disco interno si stacca può potenzialmente causare un evento trombotico e/o embolico.

#### Precauzioni

1. La procedura di posizionamento di FemoSeal™ Vascular Closure System deve essere eseguita da medici con un'adeguata formazione sull'uso del dispositivo.
2. Prima di posizionare FemoSeal™ Vascular Closure System, eseguire un angiogramma femorale limitato o una puntura femorale ecoguidata.



3. Interrompere la procedura in caso di:
  - Diametro del lume dell'arteria femorale comune < 5 mm.
  - Stenosi e/o placca significativa presente in prossimità del sito di venipuntura dell'arteria femorale comune.
  - La puntura dell'arteria avviene in corrispondenza o in posizione distale rispetto alla biforcazione dell'arteria femorale.
  - Rami anomali o alterazioni dei vasi presenti in prossimità del sito di venipuntura dell'arteria femorale comune.
4. In presenza di ematomi, prestare particolare attenzione al corretto inserimento dell'introduttore con alloggiamento a cono nell'arteria.
5. Utilizzare una tecnica di venipuntura in una sola parete. Non perforare la parete posteriore dell'arteria.
6. Adottare sempre una tecnica sterile quando si utilizza FemoSeal™ Vascular Closure System.
7. FemoSeal™ Vascular Closure System è un prodotto monouso e non deve essere risterilizzato o riutilizzato. L'unità FemoSeal™ è progettata in modo tale da non poter essere riutilizzata.
8. Se il posizionamento del sigillo interno incontra una resistenza inaspettata, interrompere la procedura.
9. Per un corretto posizionamento del sigillo interno, riposizionare il pollice in modo che il pulsante possa scattare liberamente.
10. Assicurarsi che la punta dell'introduttore con alloggiamento a cono dell'unità FemoSeal™ sia sotto la superficie cutanea prima di posizionare il disco di bloccaggio esterno. Il disco di bloccaggio esterno può essere inavvertitamente posizionato al di sopra del livello della cute in pazienti con una distanza ridotta tra l'arteria femorale e il livello della cute.
11. Per un corretto posizionamento, può essere necessaria un'incisione cutanea prima del posizionamento.
12. Se il sigillo interno è all'interno dell'arteria, ma non è possibile premere completamente il pulsante e posizionare il disco di bloccaggio esterno, può essere necessario un intervento chirurgico per rimuovere gli elementi di chiusura FemoSeal™.
13. Nel caso in cui si debba ripungere la stessa arteria femorale entro 18 mesi, pungere a 1 cm prossimale rispetto al precedente sito di accesso del FemoSeal™ Vascular Closure System.

14. Indicare al paziente di seguire le indicazioni del medico riguardo all'ispezione del sito di chiusura

15. e di portare con sé la Scheda informativa per il paziente per i 18 mesi successivi

### **Precauzioni al momento della dimissione**

Prima della dimissione, valutare le seguenti condizioni cliniche del paziente:

1. Emorragia e/o ematoma nel sito di chiusura.
2. Dolore alla deambulazione.
3. Segni di infezione nel sito di chiusura.

### **1.3.3 Procedure correttive di sicurezza sul campo**

È stata intrapresa una procedura correttiva di sicurezza sul campo riguardante FemoSeal™ VCS durante il periodo compreso tra il 1° settembre 2019 e il 31 agosto 2024.

Nel 2022, Terumo ha richiamato volontariamente FemoSeal™ VCS a causa di reclami che sostenevano l'insuccesso dei test di processo e di rilascio dei lotti del prodotto FemoSeal fabbricato a Elkton per la misurazione della forza di compressione e della forza di retrazione. In totale sono stati richiamati 950 unità dalla Corea del Sud.

## **1.4 Valutazione clinica e follow-up clinico post-vendita**

La **Tabella 1.3** include un elenco di studi cardine per la commercializzazione di FemoSeal™ VCS, nonché studi post-commercializzazione e attività di follow-up clinico post-commercializzazione. La versione del dispositivo utilizzata nello studio è inclusa nella tabella seguente. La prima versione di FemoSeal™ VCS (n. 11200) è stata lanciata sul mercato fino al 2006, mentre la versione successiva (n. C11202) è stata lanciata sul mercato nel 2006 ed è quella attualmente in commercio.

**Tabella 1.3 Riepilogo degli studi cardine**

| <b>Test funzionali pre-commercializzazione sugli animali</b>                                                                                                                                                                                                            | <b>Versione dispositivo</b> |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                       |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                       |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                       |

| <b>Primo studio clinico sull'uomo</b>                                                                                                                                                                        |                                 |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 11200                           |
| <b>Studi clinici post-commercializzazione completati</b>                                                                                                                                                     |                                 |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                   | C11202<br>(dispositivo attuale) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                            | C11202<br>(dispositivo attuale) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                                                                                               | C11202<br>(dispositivo attuale) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)                                                                                       | C11202<br>(dispositivo attuale) |
| <b>Studi clinici post-commercializzazione pianificati/in corso</b>                                                                                                                                           |                                 |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                                                                                                   | C11202<br>(dispositivo attuale) |
| <b>Attività di follow-up clinico post-commercializzazione</b>                                                                                                                                                |                                 |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                                                                                                    | C11202<br>(dispositivo attuale) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                                                                                                           | C11202<br>(dispositivo attuale) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024)                                                                              | C11202<br>(dispositivo attuale) |

#### 1.4.1 Riepilogo dei dati di pre-commercializzazione (indagini cliniche e dei test sugli animali)

La seguente **Tabella 1.4** descrive tutti gli studi pre-commercializzazione, sia i test sugli animali che le indagini cliniche.

**Tabella 1.4 Riepiloghi degli studi di pre-commercializzazione**

| Test funzionali pre-commercializzazione sugli animali                                                                                                                                                                                                                   |                                                                      |                                            |                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------|--------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Nome dello studio                                                                                                                                                                                                                                                       | Anno/CI                                                              | Tipo di studio                             | Obiettivi                                                                                                                                                                                                                                                                          | Tappe fondamentali                                                                                                                                                                                                                                                                                                                                                               | Potenziali criteri di accettazione                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 2000<br>Radi Medical System AB<br><br>Eseguito da Biomatech, Francia | Studio sugli animali; indagine esplorativa | Lo scopo dello studio era quello di valutare la biocompatibilità e la biofunzionalità di un impianto biodegradabile progettato per ottenere l'emostasi nel sistema vascolare. Il rapporto riguarda gli animali di riserva dello studio numero di studio 862 (Documento n. 1051-01) | N = 3 pecore femmine adulte, 1 animale per punto temporale<br><br>Follow-up per analisi istopatologiche, classificazione macroscopica e analisi ultrastrutturale<br><br><ul style="list-style-type: none"> <li>12 mesi</li> <li>15 mesi</li> <li>18 mesi</li> </ul><br>Follow-up ecografico Color Doppler - 30 giorni presso i siti di accesso dell'arteria carotidea e femorale | Pervietà arteriosa <ul style="list-style-type: none"> <li>Valutazione della portata di sangue dopo il posizionamento: riduzione della portata di sangue di 2/3 associata a vasospasmo arterioso temporaneo attribuito alla procedura, entrambi verificatisi a livello dell'arteria carotidea comune sinistra</li> <li>Valutazione ecografica Color Doppler (4 settimane): 3/3 (100%) senza riduzione significativa della portata di sangue 30 giorni dopo l'impianto</li> </ul><br>Osservazioni macroscopiche <ul style="list-style-type: none"> <li>12 mesi: pervietà confermata macroscopicamente dall'assenza di occlusione anatomicamente visibile; nessuna lesione macroscopica locale da intolleranza (emorragia, necrosi o neovascolarizzazione); incapsulamento del disco interno evidente</li> <li>15 mesi: l'osservazione macroscopica non ha mostrato segni di infiammazione; nessun residuo di dischi interni o esterni identificato; il tessuto di incapsulamento situato nell'area del disco esterno è apparso uguale all'osservazione a 12 mesi</li> <li>18 mesi: l'osservazione macroscopica non ha mostrato segni di intolleranza locale, disco esterno visibile (3/3 casi), degradazione del disco interno completo; 1/3 (arteria carotidea comune sinistra) - depressione della parete arteriosa osservata nel sito di impianto</li> </ul> |

|                                                                                                                                                                                                                                                                                |                                                                          |                                                   |                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|---------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                                                                                                |                                                                          |                                                   |                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                              | <p>(potrebbe essere correlata al posizionamento del dispositivo)</p> <p>Conclusioni</p> <ul style="list-style-type: none"> <li>• Macroscopicamente, a 12, 15 e 18 mesi dall'impianto, non sono stati rilevati segni necrotici, degenerativi o trombotici.</li> <li>• Il processo di degradazione dei dischi interni ed esterni si è verificato tra i 12 e i 18 mesi ed è risultato completo a 18 mesi, con un tessuto biancastro che ricopriva l'area impiantata.</li> <li>• Istologicamente, dopo 18 mesi, il materiale polimerico non era più visibile, ma era presente un tessuto fibroso endoluminale. Non sono state notate lesioni necrotiche, degenerative o trombotiche.</li> </ul>                                                                                         |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002 Radi Medical System AB</p> <p>Eseguito da Biomatech, Francia</p> | <p>Studio sugli animali; indagine esplorativa</p> | <p>Lo scopo dello studio era valutare la biocompatibilità di un impianto biodegradabile per ottenere l'emostasi nel sistema vascolare.</p> | <p>Follow-up (dopo l'impianto)</p> <ul style="list-style-type: none"> <li>• 12 settimane</li> <li>• 24 settimane</li> <li>• 36 settimane</li> </ul> <p>N = 12 pecore, 3 animali per punto temporale, 3 animali di riserva sacrificati a 12, 15 e 18 mesi</p> <p>Siti di impianto: arterie femorali destra e sinistra, arterie carotidee comuni destra e sinistra</p> <p>Analisi ecografica Color Doppler</p> | <p><u>Pervietà delle arterie carotidee e femorali dopo 4 settimane</u></p> <ul style="list-style-type: none"> <li>• Riduzione importante della portata di sangue 0/12 (0%)</li> </ul> <p><u>Nessuna riduzione importante della portata di sangue</u></p> <ul style="list-style-type: none"> <li>• Grave compromissione della portata di sangue correlata all'inserimento del dispositivo 0/12 (0%)</li> <li>• Riduzione della portata di sangue nella carotide comune sinistra 2/12 (16,6%) dovuta a vasospasmo arterioso temporaneo (attribuito all'intervento chirurgico, non al dispositivo)</li> </ul> <p><u>Compromissione della portata di sangue a seguito del follow-up</u></p> <p>12 settimane - 0/12 (0%)<br/> 24 settimane - 0/12 (0%)<br/> 36 settimane - 0/12 (0%)</p> |

|  |  |  |  |  | <p>Misurazioni della pressione sanguigna (3 pecore - 36 settimane)</p> <ul style="list-style-type: none"> <li>Nessuna riduzione importante della portata di sangue rilevata</li> </ul> <p>Dati macroscopici per integrazione e degradazione (Grado 0-4)</p> <p><u>Siti carotidei</u></p> <p><i>Lato interno</i></p> <p>-incapsulamento</p> <p>12 settimane 1,3</p> <p>24 settimane 0,8</p> <p>36 settimane 0,7</p> <p>-degradazione dei materiali</p> <p>12 settimane 2,2</p> <p>24 settimane 2,3</p> <p>36 settimane 0,7</p> <p><i>Lato esterno</i></p> <p>-incapsulamento</p> <p>12 settimane 2,0</p> <p>24 settimane 1,0</p> <p>36 settimane 0,8</p> <p>-degradazione dei materiali</p> <p>12 settimane 2,0</p> <p>24 settimane 2,7</p> <p>36 settimane 3,2</p> <p><u>Siti femorali</u></p> <p><i>Lato esterno</i></p> <p>-incapsulamento</p> <p>12 settimane 1,0</p> <p>24 settimane 2,7</p> <p>36 settimane 1,0</p> <p>-degradazione dei materiali</p> <p>12 settimane 2,0</p> <p>24 settimane 2,4</p> <p>36 settimane 3,0</p> <p><i>Lato interno</i></p> <p>-incapsulamento</p> <p>12 settimane 2,0</p> <p>24 settimane 1,2</p> <p>36 settimane 1,0</p> <p>-degradazione dei materiali</p> <p>12 settimane 1,0</p> <p>24 settimane 2,2</p> |
|--|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | 36 settimane 3,0                                                                                                            |
|--|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <u>Dati istologici per integrazione, degradazione e parametri infiammatori (media dei valori rilevanti, Indice 0-4) n=6</u> |
|  |  |  |  |  | <u>Siti carotidei</u>                                                                                                       |
|  |  |  |  |  | Fibrosi esterna                                                                                                             |
|  |  |  |  |  | 12 settimane - 2,3                                                                                                          |
|  |  |  |  |  | 24 settimane - 2,3                                                                                                          |
|  |  |  |  |  | 36 settimane - 1,8                                                                                                          |
|  |  |  |  |  | Neointima interna                                                                                                           |
|  |  |  |  |  | 12 settimane - 3,0                                                                                                          |
|  |  |  |  |  | 24 settimane - 2,7                                                                                                          |
|  |  |  |  |  | 36 settimane - 3,3                                                                                                          |
|  |  |  |  |  | Degradazione del materiale                                                                                                  |
|  |  |  |  |  | 12 settimane - 1,7                                                                                                          |
|  |  |  |  |  | 24 settimane - 3,0                                                                                                          |
|  |  |  |  |  | 36 settimane - 3+                                                                                                           |
|  |  |  |  |  | Parametri infiammatori (macrofagi)                                                                                          |
|  |  |  |  |  | 12 settimane - 3,0                                                                                                          |
|  |  |  |  |  | 24 settimane - 1,7                                                                                                          |
|  |  |  |  |  | 36 settimane - 1,7                                                                                                          |
|  |  |  |  |  | <u>Siti femorali</u>                                                                                                        |
|  |  |  |  |  | Fibrosi esterna                                                                                                             |
|  |  |  |  |  | 12 settimane - 1,3                                                                                                          |
|  |  |  |  |  | 24 settimane - 1,5                                                                                                          |
|  |  |  |  |  | 36 settimane - 1,7                                                                                                          |
|  |  |  |  |  | Neointima interna                                                                                                           |
|  |  |  |  |  | 12 settimane - 3,7                                                                                                          |
|  |  |  |  |  | 24 settimane - 3,3                                                                                                          |
|  |  |  |  |  | 36 settimane - 3,8                                                                                                          |
|  |  |  |  |  | Degradazione del materiale                                                                                                  |
|  |  |  |  |  | 12 settimane - 2,0                                                                                                          |
|  |  |  |  |  | 24 settimane - 3,0                                                                                                          |
|  |  |  |  |  | 36 settimane - 3+                                                                                                           |
|  |  |  |  |  | Parametri infiammatori (macrofagi)                                                                                          |
|  |  |  |  |  | 12 settimane - 3,5                                                                                                          |
|  |  |  |  |  | 24 settimane - 1,8                                                                                                          |
|  |  |  |  |  | 36 settimane - 1,8                                                                                                          |
|  |  |  |  |  | <u>Valori di pervietà istomorfologica</u>                                                                                   |
|  |  |  |  |  | Siti carotidei                                                                                                              |
|  |  |  |  |  | 12 settimane 74,0%                                                                                                          |
|  |  |  |  |  | 24 settimane 81,9%                                                                                                          |
|  |  |  |  |  | 36 settimane -89,43%                                                                                                        |

|                                                                                                                                                                                                                                                                 |                                                                          |                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
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|                                                                                                                                                                                                                                                                 |                                                                          |                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                 | <p>Siti femorali</p> <p>12 settimane - 42,2%</p> <p>24 settimane - 73,21%</p> <p>36 settimane - 78,71%</p> <p><u>Pervietà dei vasi US (media %)</u></p> <p>Sito carotideo</p> <p>12 settimane 94,6%</p> <p>24 settimane - 96,7%</p> <p>36 settimane - 94,7%</p> <p>Siti femorali</p> <p>12 settimane - 66,9%</p> <p>24 settimane - 63,6%</p> <p>36 settimane - 75,1%</p> <p>Conclusioni</p> <ul style="list-style-type: none"> <li>Non è stato rilevato alcun segno significativo di intolleranza locale (assenza di lesioni infiammatorie, necrotiche o degenerative visibili) a 12, 24 o 36 settimane</li> <li>Non sono state registrate reazioni tissutali avverse significative relative all'ospite e al dispositivo</li> <li>La degradazione dell'impianto era quasi completa a 36 settimane</li> </ul> |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France). | 2002<br><br>Radi Medical System AB<br><br>Eseguito da Biomatech, Francia | Studio sugli animali | Lo scopo dello studio era valutare la biocompatibilità e la biofunzionalità di un impianto biodegradabile progettato per ottenere l'emostasi nel sistema vascolare. Il dispositivo testato è stato progettato per penetrare nel foro di puntura delle arterie per ottenere l'emostasi. Un disco è stato inserito nel foro di puntura nell'arteria e l'altro ha chiuso il disco interno dall'esterno dell'arteria. Entrambi i dischi sono stati inseriti attraverso un kit introduttore. I dischi sono | Periodo di impianto/follow-up di 5 settimane per tutti gli animali<br><br>4 pecore, 1 maiale<br><br>14 elementi di chiusura<br><br>8 elementi di chiusura impiantati in 2 pecore<br><br>2 elementi di chiusura impiantati in 1 maiale<br><br>Quando due elementi di chiusura sono stati impiantati nella stessa | Sono stati registrati vari segni avversi (infiammazione, necrosi, emorragia o altre lesioni) o la formazione di un sottile strato pseudo-intimale. Particolare attenzione è stata dedicata all'integrazione tissutale iniziale del dispositivo, con particolare riguardo all'incapsulamento interno del disco.<br><br>Macroscopicamente, non sono stati osservati segni significativi di intolleranza locale o formazione di trombi. L'osservazione                                                                                                                                                                                                                                                                                                                                                          |



|  |  |  | <p>stati progettati per prevenire l'emorragia, per cicatrizzare la parete del vaso e infine per degradarsi ed essere assorbiti. Lo studio è stato progettato per raccogliere e analizzare i dati dopo l'impianto funzionale nella pecora e nel maiale per valutare la capacità dell'impianto di mantenere la funzione fisiologica quando viene utilizzato nel sistema circolatorio, per determinare la risposta dell'ospite e del dispositivo (integrità fisica, incapsulamento tissutale al momento del sacrificio) e per valutare la degradazione dell'impianto</p> | <p>arteria femorale, la distanza di impianto era &gt; 30 mm</p> | <p>macroscopica non ha rivelato alcuna differenza tra pecora e maiale dopo l'impianto degli elementi di chiusura nelle arterie femorali. Macroscopicamente, non sono stati osservati segni significativi di intolleranza locale o formazione di trombi. L'osservazione macroscopica non ha rivelato alcuna differenza tra pecora e maiale dopo l'impianto degli elementi di chiusura nelle arterie femorali.</p> <p>L'analisi istopatologica del sito di impianto nelle pecore non ha evidenziato reazioni avverse locali. I dischi interni ed esterni mostravano segni di degrado e in alcuni casi erano rotti in parti più piccole. I dischi interni erano completamente integrati nel tessuto neointimale. Nel maiale l'analisi istopatologica ha mostrato un numero leggermente maggiore di segni infiammatori intorno ai dischi interni ed esterni. In entrambi gli animali, il multifilamento ha mostrato segni infiammatori leggermente superiori rispetto al materiale del disco, come è normale per le suture intrecciate a causa della maggiore superficie.</p> <p>La pervietà del vaso è stata misurata dopo 5 settimane utilizzando tre metodi diversi, istomorfometrico, istomorfometrico in</p> |
|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                                                                                                                                                                                                              |                              |                                                    |                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                     | combinazione con la misurazione del diametro del vaso mediante calibro e con l'uso dell'ecografia Color Doppler. La pervietà media del vaso nelle pecore era compresa tra il 60 e l'80% a seconda del metodo (12 osservazioni). Nel maiale, invece, era compresa tra il 40 e l'80% (2 osservazioni).                                                                                                                                                                                                                                                                                                       |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|----------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Primo studio clinico sull'uomo</b>                                                                                                                                                                        |                              |                                                    |                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Nome dello studio                                                                                                                                                                                            | Anno/CI                      | Tipo di studio                                     | Obiettivi                                                                                                                                                                                                                                                                                                                           | Tappe fondamentali                                                                                                                                                                                                                                                                                                                                                                  | Potenziali criteri di accettazione                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Studio multicentrico, a braccio singolo, in aperto | L'obiettivo dello studio era quello di determinare la sicurezza, le prestazioni e l'efficacia di FemoSeal Vascular Closure System (FemoSeal System) in generale, e in particolare degli elementi di chiusura, in pazienti sottoposti a procedure di cardiologia diagnostica o interventistica tramite accesso all'arteria femorale. | Studio in 2 parti<br><br>Totale n = 80<br>Parte 1 n = 20<br>Parte 2 n = 60<br><br>Indicazioni:<br>Parte 1: cateterizzazione cardiaca diagnostica utilizzando l'arteria femorale come sito di accesso<br><br>Parte 2: pazienti sottoposti a procedure cardiache diagnostiche e interventistiche che utilizzano l'arteria femorale come sito di accesso<br><br>30 giorni di follow-up | Risultati<br><br><u>-emostasi ottenuta con FS senza compressione</u><br><br>- Parte 1 20/20 (100%)<br>- Parte 2 58/60 (97%)<br><br>Tempo mediano all'emostasi al momento della procedura (parte 2): 1,0 minuti (intervallo immediato - 8 minuti)<br><br><u>Tempo per la deambulazione (minuti)</u><br><br>Parte 1 -<br>Valore mediano: 33,0<br>media: 67,8<br>Parte 2 -<br>valore mediano: 45<br>media: 87,5<br><br><u>Incidenza delle complicanze vascolari maggiori - follow-up a 30 giorni</u><br><br>Parte 1<br>-Senza complicanze vascolari 20/20 (100%)<br>Parte 2<br>Pseudoaneurisma - 1/59 (1,69%) |

|  |  |  |  |  | <u>Fallimento del trattamento</u><br>Parte 1 - 0/20 (0%)<br>Parte 2 - 3/60 (5%) <ul style="list-style-type: none"> <li>• 2 a causa del mancato raggiungimento dell'emostasi senza l'uso della compressione</li> <li>• 1 a causa di una grave complicanza vascolare, pseudoaneurisma</li> </ul> |
|--|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <u>Trasudazione persistente</u><br>Parte 1 - 0/20 (0%)<br>Parte 2 - 8/60 (13%)                                                                                                                                                                                                                 |
|  |  |  |  |  | <u>Ematoma</u><br>Parte 1 - 0/20 (0%)<br>Parte 2 - 6/60 (10%)                                                                                                                                                                                                                                  |

Nell'ambito del piano di sviluppo pre-commercializzazione di FemoSeal™ VCS, sono stati completati tre test funzionali sugli animali. Nel 2000, prima di iniziare gli studi clinici, è stato eseguito uno studio sugli animali per valutare la biofunzionalità di FemoSeal™ VCS. Questo studio ha valutato la capacità degli elementi di chiusura di mantenere la funzionalità fisiologica e il loro degrado. A 18 mesi il materiale del disco interno ed esterno non era più visibile, essendo stato sostituito da un tessuto fibroso endoluminale. In conclusione, è stata confermata la capacità dell'elemento di chiusura FemoSeal™ VCS di mantenere la funzionalità fisiologica quando viene utilizzato nel sistema circolatorio.

Nel 2002 è stato condotto uno studio sugli animali per valutare la biocompatibilità e la biofunzionalità di un impianto biodegradabile, FemoSeal™ VCS, progettato per ottenere l'emostasi nel sistema vascolare. In sintesi, la degradazione dell'impianto era quasi completa a 36 settimane e non si sono verificate reazioni tissutali avverse significative.

Un altro studio condotto sugli animali nel 2002 ha valutato la biocompatibilità e la biofunzionalità di un impianto biodegradabile, FemoSeal™ VCS, progettato per ottenere l'emostasi nel sistema vascolare. Dopo 5 settimane, l'incapsulamento del disco era completo e sono stati osservati segni di degradazione dei dischi interni ed esterni. In conclusione, è stata confermata la capacità dell'impianto di mantenere la funzione fisiologica quando utilizzato nel sistema circolatorio.

Nell'ambito del piano di sviluppo clinico per FemoSeal™ VCS, Radi Medical System AB ha condotto un'indagine clinica pre-commercializzazione. Questa indagine clinica non è pubblicata né disponibile online. Lo studio con il dispositivo modello n. 11200 è stato condotto nel 2002-2004 secondo la norma europea EN 540 (Indagine clinica dei dispositivi medici per soggetti umani) e in conformità alle Considerazioni generali ICH per le sperimentazioni cliniche e alle Linee guida di buona pratica clinica. I dettagli di questo studio sono documentati nel rapporto EU-SE-001. La sperimentazione clinica è stata documentata nel rapporto finale di Radi Medical Systems AB, "Multi-Centre Clinical Trial of the FemoSeal™ Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures". Lo studio clinico è stato effettuato con il primo modello di FemoSeal n. 11200 e si è concentrato sulla sicurezza e sull'efficacia dei componenti di chiusura impiantabili. L'unica differenza tra il primo modello n. 11200 e il modello attuale, C11202, è la misura di French, rispettivamente 6 F e 7 F, e il sistema di posizionamento migliorato. I benefici clinici, l'uso previsto, i principi di funzionamento e le materie prime degli elementi di chiusura impiantabili, il disco sigillante interno e il disco di bloccaggio esterno rimangono invariati.

L'uso previsto del dispositivo era destinato ai pazienti sottoposti a procedure diagnostiche o interventistiche cardiache che utilizzavano l'arteria femorale come punto di accesso. L'obiettivo di questo studio era determinare la sicurezza, le prestazioni e l'efficacia di FemoSeal™ VCS. Si trattava di uno studio prospettico, multicentrico, in aperto, a braccio singolo, con follow-up di 30 giorni.

L'endpoint primario di performance era il tempo di emostasi, definito come l'assenza di sanguinamento acuto. L'endpoint di sicurezza primario era l'incidenza di complicanze vascolari gravi a 30 giorni. Gli endpoint secondari includevano il tempo per la deambulazione, la percentuale di fallimento del trattamento, l'incidenza di eventi avversi e le caratteristiche di prestazione del dispositivo durante l'erogazione e il posizionamento.

I pazienti inclusi in questo studio erano adulti in grado di fornire il consenso informato e con almeno un polso pedidio intatto. I pazienti sono stati esclusi dallo studio se presentavano una delle seguenti condizioni:

- Anamnesi di vasculopatia periferica
- Malattia autoimmune
- Disturbo emorragico noto o anemia grave
- INR >1,5
- Infarto miocardico a 72 ore
- Ipertensione non controllata nonostante il trattamento
- Obesità che impedisce l'accesso con la tecnica di Seldinger

- Presenza di innesto o stent vascolare nel sito dell'arteriotomia
- Precedente puntura omolaterale nei 3 mesi precedenti
- Aspettativa di vita <6 mesi

Inoltre, i pazienti sono stati esaminati in sede intraoperatoria ed esclusi dallo studio se è stato osservato uno dei seguenti fattori:

- Diametro del lume dell'arteria femorale comune <5 mm
- Rami arteriosi nel raggio di 2 cm in prossimità del sito di venipuntura
- Stenosi significativa nel raggio di 3 cm in prossimità del sito di venipuntura
- Uso del kit introduttore primario >6 Fr
- Puntura in corrispondenza o distalmente alla biforcazione femorale
- Punture femorali multiple
- Puntura nota o sospetta della parete femorale posteriore
- Ematoma di grandi dimensioni (2:6 cm) al termine della procedura
- Difficoltà di inserimento dell'introduttore primario per la procedura a causa di tessuto o vaso tortuoso

Questo studio a protocollo singolo è stato condotto in due parti: Durante la Parte 1 sono stati selezionati 20 pazienti, poi è stata completata l'analisi della sicurezza e quindi sono stati selezionati altri 60 pazienti nella Parte 2.

Nella Parte 1, l'età media dei pazienti selezionati era di 65,9 anni, il 70,0% dei pazienti era di sesso maschile e il 95% dei pazienti assumeva farmaci concomitanti. Nella Parte 2 dello studio, l'età media era di 63,8 anni, il 78% era di sesso maschile e il 100% assumeva farmaci concomitanti.

I pazienti sottoposti a procedure diagnostiche (Parte 1 e Parte 2) o interventistiche (Parte 2) di cateterizzazione cardiaca sono stati ammessi allo studio. Le procedure sono state conformi allo standard di trattamento in ciascuno degli ospedali che hanno effettuato la selezione, seguite dall'uso di FemoSeal™ VCS. I dati dei pazienti sono stati raccolti al basale, durante la procedura e a 1 giorno e 30 giorni dopo la procedura. I risultati sono riassunti nella **Tabella 1.5** e indicano che FemoSeal™ VCS è sicuro ed efficace per l'uso in questa categoria di pazienti.

**Tabella 1.5 Risultati clinici riportati in uno studio pre-commercializzazione**

|                                                                                                                      | Parte 1     | Parte 2                  |
|----------------------------------------------------------------------------------------------------------------------|-------------|--------------------------|
| Numero di pazienti                                                                                                   | 20          | 60                       |
| Tempo medio per l'emostasi                                                                                           | 1,2 minuti  | 1,6 minuti <sup>a</sup>  |
| Tempo medio per la deambulazione                                                                                     | 72,2 minuti | 87,5 minuti <sup>b</sup> |
| Incidenza delle complicanze vascolari gravi <sup>c</sup>                                                             | 0 (0%)      | 1 (2%)                   |
| Numero di pazienti con eventi avversi                                                                                | 5 (25%)     | 19 (32%)                 |
| Fallimento del trattamento (definito come complicanze vascolari gravi, necessità di compressione manuale o entrambe) | 0 (0%)      | 3 (5%)                   |
| Malfunzionamenti del dispositivo                                                                                     | 0 (0%)      | 6 (10%)                  |

<sup>a</sup>Sulla base di un campione totale di 58 pazienti, 2 non hanno raggiunto l'emostasi al momento della procedura a causa di precedenti punture omolaterali. L'emostasi è stata ottenuta a 7 minuti e a 37 minuti per questi pazienti.

<sup>b</sup>Sulla base di un campione totale di 59 pazienti: 1 paziente non è stato incluso perché è stato inserito nel respiratore a causa di un edema polmonare e non è stato in grado di deambulare per oltre una settimana.

<sup>c</sup>Definita come complicanza vascolare che richiede la trasfusione di sangue o la riparazione chirurgica, o infezione locale che richiede la somministrazione di antibiotici, il ricovero o l'estensione del ricovero, o il debridement del sito

Non sono state osservate complicanze vascolari gravi nella Parte 1 dello studio. Nella Parte 2 dello studio è stata segnalata una complicanza vascolare grave: pseudoaneurisma riportato a un giorno dalla procedura. L'evento ha richiesto una compressione ecoguidata e un'iniezione di trombina nello pseudoaneurisma, prolungando il ricovero del paziente.

Dei cinque eventi avversi riportati nella Parte 1 dello studio, si è verificato un possibile evento avverso correlato al dispositivo: un evento non grave di sanguinamento acuto a 1 giorno dall'intervento. Dei 19 eventi avversi riportati nella Parte 2 dello studio, sono stati osservati tre eventi avversi non gravi legati al dispositivo, come ematomi, e sei eventi non gravi probabilmente legati al dispositivo, tra cui tre segnalazioni di trasudamento persistente, due ematomi e un dolore alla gamba dopo l'esercizio fisico.

Nella Parte 2 erano presenti tre pazienti considerati fallimenti del trattamento: due a causa del mancato raggiungimento dell'emostasi senza l'uso della compressione e uno a causa della complicità vascolare maggiore (pseudoaneurisma). Nella Parte 1 dello studio non sono stati riscontrati fallimenti nel trattamento.

Dei sei malfunzionamenti del dispositivo nella Parte 2 dello studio, tre non hanno interferito con la procedura, uno è stato attribuito a un errore dell'operatore, uno a perdite dell'introduttore e uno alla rottura del filamento. Gli ultimi due problemi sono stati affrontati con gli aggiornamenti dei modelli implementati in C11202.

La Parte 2 dello studio clinico pre-commercializzazione non ha riportato i risultati del follow-up a 6 mesi a causa della mancata rispondenza del paziente. I risultati dello studio clinico pre-commercializzazione (EU-SE-001) di 30 giorni, in linea con il periodo di tempo di follow-up della letteratura clinica, dimostrano che FemoSeal™ VCS è sicuro ed efficace.

#### 1.4.2 Riepilogo dei dati degli studi clinici post-commercializzazione

Sono stati completati quattro studi clinici post-commercializzazione descritti nella **Tabella 1.6** sottostante. Queste indagini cliniche non sono pubblicate né disponibili online.

**Tabella 1.6 Studi clinici post-commercializzazione**

| Studi clinici post-commercializzazione completati                                           |              |                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                            |
|---------------------------------------------------------------------------------------------|--------------|--------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Nome dello studio                                                                           | Anno/CI      | Tipo di studio                                                                             | Obiettivi                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Tappe fondamentali                                                                                                                                                                                                                                                                                                                                    | Potenziati criteri di accettazione                                                                                                                         |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI | Studio post-commercializzazione, accettabilità da parte dell'utente della nuova confezione | Studio post-commercializzazione effettuato sull'aggiornamento del modello FemoSeal Vascular® Closure System n. 11202 che presenta un sistema di posizionamento modificato rispetto al primo modello, n. 11200, per documentare la funzionalità.<br><br>L'obiettivo dello studio era ottenere un feedback sulle Istruzioni per l'uso (IFU) riviste, sul progetto di formazione per medici e infermieri, per confermare le valutazioni effettuate nell'analisi dei rischi e per fornire input per eventuali miglioramenti della qualità dei prodotti. | 100 pazienti <ul style="list-style-type: none"> <li>63 uomini/37 donne</li> <li>Età media 68 anni per le donne, 65 per i maschi</li> </ul> 2 ospedali svedesi, 6 medici<br><br>112 dispositivi<br><br>Dati acquisiti sui moduli di registrazione dei pazienti (CRF)<br><br>Tempo di osservazione pianificato: 30 minuti dal momento dell'applicazione | Risultati<br><br>1. Illustrazioni/istruzioni contenute nelle Istruzioni per l'uso considerate informative e adeguate<br><br>2. Emostasi immediata (91/100) |

|                                                                                   |                                                           |                                                  |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                              |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
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| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008) | Dott. Nicolas Moes, Innsbruck Medical University, Austria | Valutazione di conferma post-commercializzazione | L'obiettivo di questo studio era valutare la sicurezza e le prestazioni di FemoSeal® utilizzato durante la normale routine clinica in pazienti sottoposti a cateterizzazione cardiaca diagnostica o procedura di intervento cardiaco percutaneo eseguita con introduttore 7 F. | 50 pazienti consecutivi<br><br>Indicazione - cateterizzazione cardiaca diagnostica o invasiva dall'arteria femorale comune<br><br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.6±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                                                                                                                                                            | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.6±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Endpoint primari <ul style="list-style-type: none"><li>Endpoint primario di efficacia - TTH (tempo di emostasi) con o senza trasudazione ma senza compressione aggiuntiva, manuale o meccanica.</li><li>Endpoint di sicurezza - incidenza di eventi avversi - complicanze vascolari minori e gravi e tutti gli altri eventi avversi gravi e non gravi durante lo studio (ovvero fino alla dimissione del paziente).</li></ul> Risultati <ul style="list-style-type: none"><li>Tempo medio per l'emostasi</li><li>Diagnostica - 56,6 ± 29 secondi</li><li>Intervento 59,9 ± 16,2 secondi</li><li>Tutti i pazienti 57,8 ± 26,3</li><li>Tutti i pazienti sono stati in grado di deambulare senza problemi dopo 4 ore di riposo a letto.</li></ul> Risultati in termini di sicurezza <ul style="list-style-type: none"><li>49/50 (98%) senza complicanze vascolari fino alla dimissione dall'ospedale</li><li>Tempo medio di dimissione 2,6 giorni</li><li>1/50 (2%) sanguinamento minore il giorno successivo dopo una deambulazione senza problemi il giorno dell'angiografia</li></ul> |
| n                                                                                 | 50                                                        |                                                  |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                              |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| men                                                                               | 35 (70%)                                                  |                                                  |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                              |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| women                                                                             | 15 (30%)                                                  |                                                  |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                              |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| PCI cases                                                                         | 15                                                        |                                                  |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                              |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| age (yrs)                                                                         | 62.6±11.1                                                 |                                                  |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                              |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| body mass index (kg/m²)                                                           | 25.4±6.7                                                  |                                                  |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                              |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| systolic BP (mmHg)                                                                | 131.2±20.9                                                |                                                  |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                              |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| diastolic BP (mmHg)                                                               | 77.9±10.6                                                 |                                                  |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                              |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| diabetes mellitus                                                                 | 9 (18%)                                                   |                                                  |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                              |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| arterial hypertension                                                             | 34 (68%)                                                  |                                                  |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                              |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| previous coronary intervention                                                    | 13 (26%)                                                  |                                                  |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                              |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| preprocedure aspirin                                                              | 50 (100%)                                                 |                                                  |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                              |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| preprocedure clopidogrel                                                          | 50 (100%)                                                 |                                                  |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                              |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Procedural unfractionated heparin                                                 | 15 (30%)                                                  |                                                  |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                              |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Procedural abciximab                                                              | 2 (4%)                                                    |                                                  |                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                              |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)    | 2009 RADI                                                 | Studio post-commercializzazione                  | Lo studio deve informare se i clienti/utenti hanno percepito eventuali problemi con la nuova confezione, in particolare il lato esterno non sterile della busta Tyvek/PET-PE.                                                                                                  | 25 dispositivi<br><br>4 ospedali svedesi<br><br>16/25 (64%) pazienti sottoposti a intervento coronarico percutaneo con forti farmaci anticoagulanti                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Risultati<br>1. Problemi relativi alla confezione - 21/25 (84%) applicazioni sono andate a buon fine; 4/25 (16%) non sono andate a buon fine (1 - test di un nuovo kit introduttore, 1 disco interno ha attraversato l'arteriotomia nella fase di appoggio, il pulsante si è |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |



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|----------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|-----------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                        |                                        |                                                                             | <p>Lo studio deve inoltre fornire informazioni sul fatto che il medico curante percepisca eventuali divergenze nei livelli di applicazione/posizionamento del dispositivo rispetto ai dispositivi utilizzati in precedenza.</p> <p>Lo studio deve inoltre fornire informazioni su eventuali ulteriori esigenze di miglioramento della qualità dei prodotti.</p> |                                                                                                                                                                                                                                                                                                                                                                                                                                                     | <p>sollevato e il disco esterno è stato posizionato nel canale del tessuto di incisione, 2 emostasi immediate non sono state raggiunte nonostante l'assenza di problemi di posizionamento)</p> <p>2. Emostasi immediata 19/25 (76%) pazienti</p> <p>3. Emorragia 11/25 (44%) - 9/25 (36%) trasudazione/emorragia, 2/25 (8%) ematomi</p> <p>Tasso totale di eventi 19%</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <p>The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022)</p> | <p>2022/Terumo Medical Corporation</p> | <p>Prospettico, multicentrico, osservazionale, post-commercializzazione</p> | <p>Dimostrare ulteriormente la sicurezza e l'efficacia di FemoSeal™ VCS nel raggiungimento dell'emostasi del sito di accesso all'arteria femorale comune (CFA) in soggetti reali sottoposti a procedure endovascolari percutanee</p>                                                                                                                            | <ul style="list-style-type: none"> <li>Follow-up del paziente a 30 giorni (<math>\pm 7</math> giorni) tramite visita ospedaliera o telefonata.</li> <li>Ammissione: da dicembre 2021 a luglio 2022.</li> <li>230 soggetti ammessi sottoposti a procedure diagnostiche o interventistiche endovascolari in cui è stato utilizzato FemoSeal™.</li> </ul> <p>3 siti europei: Francia (92 pazienti), Germania (38 pazienti), Belgio (100 pazienti).</p> | <ul style="list-style-type: none"> <li><b>Dati demografici/comorbidità:</b> <ul style="list-style-type: none"> <li>- Genere: 161 maschi (70%)/69 femmine (30%).</li> <li>- Età media: <math>70 \pm 12</math>.</li> <li>- IMC: <math>26,1 \pm 4,95</math> kg/m<sup>2</sup>.</li> <li>- Ipertensione: 160 pazienti (69,6%).</li> <li>- Dislipidemia: 128 (55,7%).</li> <li>- Coronaropatia: 42 (18,3%).</li> <li>- Fumatore attuale: 86 (37,6 %).</li> <li>- Fumatore passato: 66 (28,8%).</li> <li>- Cardiopatia coronarica: 34 (14%).</li> <li>- Infarto miocardico acuto: 18 (7,8%).</li> <li>- Rivascolarizzazione dell'arteria periferica 12 (5,2%) carotide e 83 (37,5%) arteria dell'arto inferiore.</li> <li>- Terapia antiaggregante (al basale): 211 (91,7%), tra cui 21 (9,1%) duplice terapia antiaggregante (DAPT).</li> <li>- Anticoagulazione orale: 40 (17,4%) pazienti.</li> </ul> </li> <li><b>Caratteristiche dell'intervento:</b></li> </ul> |

|  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
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|  |  |  |  |  | <ul style="list-style-type: none"> <li>- Ambito: clinica ospedaliera 162 casi (70,4%), clinica ambulatoriale 68 casi (29,6%).</li> <li>- Indicazione prevalente: claudicazione 147 casi (63,9%).</li> <li>- Metodologia: 35 anterogradi (15,3%), 194 retrogradi (84,7%).</li> <li>• <b>Endpoint primari:</b> <ul style="list-style-type: none"> <li>- L'endpoint combinato di sicurezza (assenza di complicanze maggiori dell'arto del sito di accesso entro 6 ore dalla procedura) e di efficacia (emostasi del sito di venipuntura riuscita) è stato raggiunto in 215/226 (95,1%) [95% CI: 91,46; 97,55] pazienti nel set di analisi completo e 215/230 (93,5%) [CI al 95% 89,47, 96,30] nel set trattato FemoSeal™.</li> <li>- L'endpoint di efficacia è stato raggiunto in 219/226 (96,9%) CI [93,7, 98,7] pazienti.</li> <li>- Endpoint di sicurezza raggiunto in 220/230 (95,2%) [CI al 95%: 92,15, 97,90] pazienti.</li> </ul> </li> <li>• <b>Endpoint secondari:</b> <ul style="list-style-type: none"> <li>- L'assenza di complicanze minori nel sito di accesso per sei ore post-procedura è stata ottenuta in 225/230 (97,8%) [CI 95%: 95,00; 99,29].</li> <li>- L'assenza di complicanze maggiori e minori del sito di accesso da sei ore a 30 giorni post-procedura è stata ottenuta in 219/230 (95,2%) [CI 95%:91,60; 97,59] pazienti.</li> <li>- Tempo mediano per l'emostasi con</li> </ul> </li> </ul> |
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|  |  |  |  |  | <p>FemoSeal™ VCD: 0,42 (0,25; 0,50) minuti.</p> <p>- Tempo mediano per la deambulazione: 5,00 (4,54; 5,50) minuti.</p> <p>- Durata media della degenza ospedaliera: 23,98 (22,72, 25,00) ore.</p> <p>- Usabilità di FemoSeal™ VCS: "facile" o "molto facile" da posizionare nel 98,7% dei casi ("facile" da posizionare in 21 (9,2%) casi, "molto facile" da posizionare in 205 (89,5%) casi) con nessuna o bassa resistenza al posizionamento nel 226 (98,3%) dei casi.</p> <p>152/230 (66,1%) pazienti trattati con il filo guida incluso nel kit FemoSeal™ (GW 0,038") e raccomandato in FemoSeal™ senza alcuna deficienza del dispositivo o evento avverso segnalati.</p> |
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Lo studio del 2006 è stato condotto per confermare la sicurezza e l'efficacia dell'attuale dispositivo con un sistema di erogazione migliorato e per ottenere un feedback sulle Istruzioni per l'uso e sul programma di formazione FemoSeal™ VCS. Lo studio ha incluso 100 pazienti e l'endpoint primario è stato il raggiungimento dell'emostasi o la necessità di ulteriori compressioni manuali o meccaniche. Questo studio ha concluso che l'applicazione di FemoSeal™ VCS è andata a buon fine nella maggior parte dei casi (il 91% ha ottenuto un'emostasi immediata).

Lo studio del 2008 ha selezionato 50 pazienti per valutare la sicurezza e le prestazioni di FemoSeal™ VCS quando viene utilizzato durante la normale routine clinica in pazienti sottoposti a una cateterizzazione cardiaca con un introduttore da 7 Fr. L'endpoint primario dello studio era la raccolta di dati sul tempo di emostasi e sul tempo per la deambulazione senza ulteriori compressioni, manuali o meccaniche. I risultati dello studio hanno concluso che il tempo medio di emostasi è stato di 57,8 secondi e tutti i pazienti sono stati in grado di deambulare dopo 4 ore di riposo a letto.

Lo studio del 2009 è stato condotto per valutare la nuova confezione FemoSeal™ VCS. Nello studio sono stati selezionati 25 pazienti. L'endpoint primario era quello di stabilire se l'utente avesse riscontrato problemi con la confezione. Gli utenti non hanno riscontrato problemi relativi

alla nuova confezione FemoSeal™ VCS. Questo studio ha anche raccolto dati per il tempo di emostasi.

Lo studio 2022 si proponeva di raccogliere in modo proattivo i dati di sicurezza ed efficacia di FemoSeal VCS nel raggiungere l'emostasi del sito di accesso all'arteria femorale comune (CFA) in soggetti reali sottoposti a procedure endovascolari percutanee. Allo studio sono stati ammessi 230 pazienti. Gli endpoint primari per lo studio di registro sono il successo procedurale (ovvero emostasi del sito di venipuntura riuscita) e la riduzione di complicazioni gravi (ad es. lesioni vascolari, emorragia correlata al sito di accesso, infezione del sito di accesso, compressione manuale ripetuta e nuova ischemia acuta della gamba omolaterale correlata al sito di accesso). Lo studio ha concluso che FemoSeal™ VCS funziona bene in ambienti reali e fornisce un'emostasi efficace e bassi tassi di complicanze nel sito di accesso per i pazienti sottoposti a interventi endovascolari periferici. Ha dimostrato buone prestazioni con un breve tempo di emostasi e un buon feedback di usabilità da parte dell'operatore, rendendo FemoSeal™ VCS un valido dispositivo per la chiusura degli accessi femorali.

### 1.4.3 Riepilogo dei dati del follow-up clinico post-commercializzazione

#### 1.4.3.1 Follow up clinici post-commercializzazione completati

Un riepilogo delle attività di follow-up clinico post-commercializzazione completate è descritto nella **Tabella 1.7** di seguito.

**Tabella 1.7. Attività di follow-up clinico post-commercializzazione**

| Attività di follow-up clinico post-commercializzazione completate         |          |                                                                          |                                                                                                                                                                                       |                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                    |
|---------------------------------------------------------------------------|----------|--------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Nome dell'attività                                                        | Anno/C I | Tipo di studio                                                           | Obiettivi                                                                                                                                                                             | Tappe fondamentali                                                                                                                               | Potenziati criteri di accettazione                                                                                                                                                                                                                                                                                                 |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021 TMC | Sondaggio clinico post-commercializzazione e - sondaggio di alta qualità | Sondaggio post-commercializzazione per raccogliere feedback prospettici relativi all'uso del dispositivo di chiusura vascolare FemoSeal™ distribuito nei mercati dell'Unione Europea. | <ul style="list-style-type: none"> <li>120 casi</li> <li>8 medici unici con &gt;5 anni di esperienza</li> <li>Diversi paesi in Europa</li> </ul> | <p><b>Valutazioni dei dispositivi in scala 1-5 - Proposte del sondaggio</b></p> <ul style="list-style-type: none"> <li>Criteri di accettazione <ul style="list-style-type: none"> <li>Le valutazioni da 3 a 5 sono considerate favorevoli</li> <li>Tutte le proposte devono avere <math>\geq 80\%</math> di</li> </ul> </li> </ul> |

| Attività di follow-up clinico post-commercializzazione completate    |          |                                                                        |                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|----------------------------------------------------------------------|----------|------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                      |          |                                                                        |                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                             | <p>feedback positivi</p> <ul style="list-style-type: none"> <li>Risultati <ul style="list-style-type: none"> <li>Nessuna proposta di sondaggio ha ricevuto più del 20% di risposte negative</li> <li>Non sono stati inoltrati reclami contro il prodotto</li> </ul> </li> </ul>                                                                                                                                                                                                                                                                    |
| 20210298 – 0.035” and 0038” Guidewire Clinical Survey Report (2021 ) | 2021 TMC | Sondaggio clinico post-commercializzazione - sondaggio di alta qualità | Sondaggio post-commercializzazione per raccogliere feedback prospettici relativi all'uso del filo guida da 0,035" incluso con Angio-Seal™ VIP Vascular Closure Device (VCD) da 6 Fr e da 0,038" incluso con Angio-Seal™ VIP VCD da 8 Fr e FemoSeal Vascular Closure System distribuito nei mercati dell'Unione Europea. | <ul style="list-style-type: none"> <li>Sondaggi per filo da 0,035" <ul style="list-style-type: none"> <li>106 sondaggi</li> <li>64 medici</li> </ul> </li> <li>Sondaggi per filo da 0,038" <ul style="list-style-type: none"> <li>109 sondaggi</li> <li>55 medici</li> </ul> </li> <li>12 sondaggi retrospettivi</li> </ul> | <p><b>Valutazioni dei dispositivi in scala 1-5 - Proposte del sondaggio</b></p> <ul style="list-style-type: none"> <li>Criteri di accettazione <ul style="list-style-type: none"> <li>Le valutazioni da 3 a 5 sono considerate favorevoli</li> <li>Tutte le proposte devono avere <math>\geq 80\%</math> di feedback positivi</li> </ul> </li> <li>Risultati <ul style="list-style-type: none"> <li>Tutti i fili guida hanno ricevuto valutazioni accettabili</li> <li>Non sono stati presentati reclami contro il prodotto</li> </ul> </li> </ul> |

| Attività di follow-up clinico post-commercializzazione completate                                                               |                     |                                                                          |                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|---------------------------------------------------------------------------------------------------------------------------------|---------------------|--------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024<br>TMC/TE | Sondaggio clinico post-commercializzazione e - sondaggio di alta qualità | per raccogliere prospetticamente feedback relativi all'uso di FemoSeal VCS con fili guida distribuiti sul mercato europeo. | <ul style="list-style-type: none"> <li>• 126 sondaggi               <ul style="list-style-type: none"> <li>• 7 siti</li> <li>• 5 paesi</li> </ul> </li> <li>• 14 novembre 2023- 11 giugno 2024</li> <li>• Specialità medica del medico:               <ul style="list-style-type: none"> <li>○ Chirurgia vascolare</li> <li>○ Radiologia interventista</li> <li>○ Angiologia</li> </ul> </li> </ul> | <b>Valutazioni dei dispositivi in scala 5 - Proposte del sondaggio</b> <ul style="list-style-type: none"> <li>• Criteri di accettazione               <ul style="list-style-type: none"> <li>○ Le valutazioni da 3 a 5 sono considerate favorevoli</li> <li>○ Tutte le proposte devono avere ≥80% di feedback positivi</li> <li>○ Se si verificano eventi avversi in questo sondaggio, devono essere quelli previsti dalla gestione del rischio.</li> </ul> </li> <li>• Dati demografici del paziente               <ul style="list-style-type: none"> <li>○ Femmina: 29,4% (37/126)</li> <li>○ Maschio: 69,8% (88/126)</li> <li>○ Sesso non dichiarato: 0,8 (1/126)</li> <li>○ Età &gt;75 anni: 31,7%</li> </ul> </li> <li>• Risultati               <ul style="list-style-type: none"> <li>○ Filo guida fornito con FemoSeal™ VCS: 101/126 (80,2%).</li> <li>○ Durata procedura (minuti): 63,4</li> </ul> </li> </ul> |

| Attività di follow-up clinico post-commercializzazione completate |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|-------------------------------------------------------------------|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                   |  |  |  |  | (36,6) (media (SD)); 57,0 (36,0-81,0) (mediana (IQR)) <ul style="list-style-type: none"> <li>○ Tutte le valutazioni delle prestazioni di FemoSeal™ VCS sono state favorevoli.</li> <li>○ Tutte le valutazioni del filo guida fornito con FemoSeal™ VCS sono state favorevoli.</li> <li>○ Un evento avverso (0,8%): i dischi FemoSeal™ VCS non erano ben allineati probabilmente a causa dell'uso di un filo guida rigido (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 pollici) che richiedeva una compressione manuale per ottenere l'emostasi.</li> </ul> |

Terumo Medical Corporation ha completato tre sondaggi di alta qualità tra gli utenti medici durante l'attuale periodo di riferimento (1° settembre 2019-31 agosto 2024).

I sondaggi clinici FemoSeal™ hanno raccolto dati clinici proattivi in relazione alla sicurezza e alle prestazioni di FemoSeal™ VCS durante l'uso clinico. Il sondaggio comprendeva domande incentrate sul dispositivo e sugli accessori associati, compreso il filo guida da 0,038", e sulle loro interazioni dirette. Le indagini cliniche sul filo guida hanno raccolto dati clinici proattivi in relazione alla sicurezza e alle prestazioni durante l'uso clinico del filo guida da 0,038" fornito con FemoSeal™ VCS. Le domande del sondaggio riguardavano specificamente l'uso generale del filo guida, dall'inserimento attraverso l'introduttore procedurale nel sistema vascolare fino alla rimozione.

FemoSeal™ VCS e il filo guida da 0,038" in dotazione al dispositivo hanno ricevuto tutte valutazioni accettabili e sono stati presentati sei (6) reclami per il dispositivo e nove (9) non reclami per il filo guida sulla base della valutazione dei commenti ricevuti dai sondaggi clinici di alta qualità. I reclami sono stati valutati sia per FemoSeal che per il filo guida nell'ambito del processo di monitoraggio post-commercializzazione di Terumo. Non sono stati individuati nuovi rischi e/o livelli di rischio.

Nel 2024 è stato completato un sondaggio tra gli utenti medici nell'ambito delle attività PMCF. I risultati del sondaggio hanno dimostrato che la valutazione delle prestazioni e la sicurezza di FemoSeal™ VCS sono state complessivamente molto favorevoli. È stata inoltre dimostrata la compatibilità di fili guida diversi da quello standard fornito con FemoSeal™ VCS.

#### **1.4.3.2 Follow-up clinico post vendita in corso/previsto**

TMC ha un'attività di follow-up clinico post-commercializzazione in corso/pianificate. Verrà completato un sondaggio clinico per raccogliere in modo prospettico il feedback relativo all'uso del filo guida con FemoSeal VCS distribuito nel mercato UE. Il sondaggio sarà completato dai medici in modo da studiare quali fili guida hanno utilizzato durante la procedura. Lo scopo di questo sondaggio è quello di colmare una lacuna identificata come la mancanza di letteratura e di commenti di revisori esterni sulla compatibilità del FemoSeal™ VCS con l'uso di altri fili guida di marche diverse da Terumo. Il feedback include risultati tecnici, prestazioni cliniche e sicurezza relativi alle prestazioni del dispositivo con fili guida diversi.

#### **1.4.4 Riepilogo dei dati della revisione sistematica della letteratura**

Terumo Medical Corporation effettua revisioni sistematiche della letteratura per raccogliere e valutare i dati sulla sicurezza clinica e sulle prestazioni derivanti da studi pubblicati su FemoSeal™ VCS e/o dispositivi simili. Lo scopo dello screening annuale della letteratura pubblicata è quello di individuare effetti collaterali precedentemente sconosciuti, monitorare gli effetti collaterali noti, individuare i rischi emergenti e individuare un possibile uso sistematico improprio o off-label di FemoSeal™ VCS.



La più recente revisione sistematica della letteratura, che ha riguardato il periodo dal 1° settembre 2019 al 31 agosto 2024, ha individuato 28 studi pubblicati che hanno fornito dati sulla sicurezza clinica e sulle prestazioni del FemoSeal™ VCS. Ventitré riferimenti hanno riportato l'uso on-label di FemoSeal™ VCS, mentre l'uso off-label è stato riportato in nove studi. Nel complesso, la revisione della letteratura su studi specifici per l'uso di FemoSeal™ VCS mostra una categoria oggetto di studio rappresentativa dei pazienti dell'UE sottoposti a procedure di cateterizzazione vascolare percutanea. Consultare la **Sezione 3** per un elenco di queste 23 pubblicazioni on-label sottoposte a peer-review.

Le prestazioni cliniche sono state valutate con le seguenti misure:

- Il tempo di emostasi è migliore o paragonabile allo stato dell'arte per la chiusura percutanea della comune arteria femorale.
- Il tempo di deambulazione è migliore o paragonabile allo stato dell'arte per la chiusura percutanea della comune arteria femorale.
- Il tasso di complicanze post-operatorie è paragonabile o inferiore agli standard di cura attuali.

Sulla base di queste misurazioni delle prestazioni cliniche, i dati riportati in questa revisione della letteratura hanno dimostrato che FemoSeal™ VCS può essere utilizzato con successo nella chiusura della puntura arteriosa femorale (arteriotomia) in pazienti sottoposti a cateterizzazione percutanea utilizzando un introduttore procedurale di massimo 7 Fr. L'emostasi completa è stata raggiunta nella maggior parte dei pazienti (79,65-100%) dei casi ed è stata associata a un tempo mediano di emostasi di 0,5 minuti, tempo medio di dimissione di 3 giorni. Tra il 69,2-86,7% dei pazienti è stato in grado di deambulare 5 ore dopo la chiusura, con un riposo postoperatorio medio a letto di 349 min. L'insuccesso di FemoSeal™ VCS è stato osservato nel 3,68-4% dei casi ed è stata necessaria un'ulteriore compressione manuale nello 0,9-4,4% delle procedure.

La sicurezza clinica è stata valutata in base a eventi avversi, tra cui, a titolo esemplificativo ma non esaustivo:

- Sanguinamento
- Ematoma
- Pseudoaneurisma
- Ematoma
- Fistola arterovenosa
- Infezione
- Decesso

Per ciascuno di questi eventi avversi, il tasso di insorgenza riportato per FemoSeal™ VCS negli studi inclusi era inferiore o paragonabile ai tassi riportati storicamente per la compressione manuale e altri dispositivi di chiusura vascolare.

Dall'esame dei 10 referti non sono stati identificati eventi avversi, in quanto non sono stati individuati rischi nuovi, imprevisti, emergenti o inaccettabili.

L'efficacia complessiva dell'uso di FemoSeal™ VCS durante l'angiografia diagnostica o le operazioni interventistiche dipende da diversi fattori quali sesso, età, anatomia del paziente, comorbidità, posizionamento anatomico del sito di venipuntura, esperienza del chirurgo, metodo di posizionamento del VCD, assistenza postoperatoria, ecc. Oltre al successo tecnico, compreso il raggiungimento dell'emostasi, FemoSeal™ VCS ha offerto benefici clinici relativi alla chiusura vascolare dopo la puntura dell'arteria femorale, come la riduzione del tempo di emostasi e del tempo alla deambulazione. I risultati delle prestazioni di FemoSeal™ VCS sono coerenti con quelli attesi per questo tipo di dispositivi se utilizzati come previsto. Alcuni dei riferimenti recuperati durante il periodo di ricerca corrente hanno mostrato l'uso del dispositivo in una posizione anatomica diversa dall'arteria femorale comune e per la chiusura di arteriotomie >7 Fr, che è considerato off-label.

Durante la revisione non sono stati identificati effetti collaterali sconosciuti, rischi emergenti o possibili usi impropri sistematici del dispositivo. Tuttavia, se FemoSeal™ VCS viene utilizzato con cautela da medici qualificati, il dispositivo medico funziona come un dispositivo clinico utile e necessario. Nel complesso, la terapia target e quindi FemoSeal™ VCS soddisfano l'esigenza clinica attualmente esistente nel trattamento delle complicanze correlate all'accesso vascolare.

Complessivamente, i dati contenuti in questa revisione della letteratura non hanno evidenziato alcun problema di prestazioni o sicurezza in ambito clinico precedentemente sconosciuto, né eventi avversi verificatisi a tassi superiori a quelli previsti/accettabili. Pertanto, da questa revisione della letteratura si può concludere che il FemoSeal™ VCS, quando viene utilizzato per fornire la compressione per l'emostasi in corrispondenza dell'arteriotomia dopo la cateterizzazione percutanea, continua a funzionare come previsto e non è associato a gravi eventi per la sicurezza.

#### **1.4.5 Riepilogo dei dati della sorveglianza post-commercializzazione**

È in vigore un sistema PMS proattivo e la revisione di tutti i reclami è completata su base mensile e in conformità con le procedure di produzione interne. I dati relativi ai reclami sono stati analizzati dal 1° settembre 2019 al 31 agosto 2024. Complessivamente, sono stati inviati al fabbricante 28 rapporti di vigilanza sui dispositivi medici (MDV) e 476 rapporti di reclami dei clienti. Dei 28 rapporti MDV, 27 erano correlati a eventi avversi e uno a malfunzionamento del dispositivo. Si sono verificati due decessi durante il periodo di riferimento, ma nessuno dei decessi segnalati è stato ritenuto correlato al dispositivo in questione. Tra i 476 reclami presentati al fabbricante, i motivi più comuni dei reclami erano le difficoltà di posizionamento (146 occorrenze, tasso di occorrenza dello 0,0142%). Guasti durante l'estrazione costituiscono il secondo motivo più frequente, con un tasso dello 0,0126% (130 eventi).

FemoSeal™ Vascular Closure System ha registrato oltre 1.030.136 vendite a livello globale e 827.843 nello Spazio Economico Europeo. La frequenza calcolata dei reclami in base alle vendite globali è dello 0,046%. Il tasso complessivo di reclami dei clienti è molto basso. Non sono stati identificati nuovi rischi rispetto a quelli inclusi nelle Istruzioni per l'uso e nella documentazione sui rischi.

I tassi di insorgenza degli effetti collaterali indesiderati sono riportati nella **Tabella 1.2**. Tramite i reclami non sono stati individuati nuovi rischi imprevisti, emergenti o inaccettabili. Non si sono verificati aumenti significativi della frequenza o della gravità degli effetti collaterali indesiderati noti.

#### 1.4.6 Riepilogo generale delle prestazioni cliniche e di sicurezza

FemoSeal™ VCS è indicato per l'uso nella chiusura della puntura dell'arteria femorale comune (arteriotomia) in pazienti sottoposti a cateterizzazione percutanea con introduttore procedurale di dimensioni pari o inferiori a 2,33 mm (7 F). Questa valutazione clinica si basa su un'analisi completa dei dati clinici e della letteratura pre- e post-commercializzazione disponibili rilevanti per l'uso previsto di FemoSeal™ VCS.

È stata condotta una revisione completa della letteratura pubblicata nel periodo compreso tra il 1° settembre 2019 e il 31 agosto 2024. Le prove raccolte comprendevano 29 studi per il FemoSeal™ VCS. Le prove fornite nella valutazione clinica concludono che, se utilizzato come indicato, il dispositivo in questione è sicuro ed efficace e che eventuali rischi o effetti collaterali indesiderati, che possono essere associati al dispositivo nelle normali condizioni d'uso, costituiscono rischi accettabili se soppesati rispetto ai benefici per il paziente. I risultati delle prestazioni dei dispositivi in esame sono coerenti con quelli attesi per questo tipo di dispositivi quando vengono utilizzati come previsto.

I potenziali effetti collaterali indesiderati associati all'uso di FemoSeal™ VCS comprendono gli eventi avversi comunemente riportati con mezzi alternativi di chiusura dell'arteriotomia, ad esempio emorragia ed ematoma. Nel complesso, i tassi di insorgenza degli eventi avversi riportati con l'uso di FemoSeal™ VCS sono simili ai tassi riportati con la compressione manuale e dispositivi di chiusura vascolare simili. Nello specifico, per l'emorragia e l'ematoma, i tassi riportati per FemoSeal™ VCS sono inferiori ai tassi riportati per dispositivi di chiusura vascolare simili. Ciascuno degli eventi avversi segnalati, sia dalla letteratura pubblicata che dal monitoraggio post-commercializzazione, è stato individuato in precedenza (vedere **Sezione 1.3**).

I dati esistenti relativi alla sicurezza clinica e alle prestazioni di FemoSeal VCS suggeriscono che i benefici per il paziente derivanti dall'uso di questo dispositivo di chiusura vascolare superano i possibili rischi quando viene utilizzato in conformità con le Istruzioni per l'uso.

Come indicato nei paragrafi precedenti, i dati forniti per FemoSeal™ VCS dimostrano la coerenza tra i dati relativi al dispositivo in esame (ad esempio utilizzo del dispositivo, risultati di

sicurezza, prestazioni cliniche e benefici clinici), quelli relativi ai dispositivi equivalenti identificati e i dati relativi a dispositivi simili elencati nello Stato dell'Arte.

L'analisi incrociata dei dati di sicurezza non ha individuato alcuna carenza tra i seguenti elementi:

- Dati citati nello stato dell'arte
- Dati specifici del dispositivo in fase di valutazione
- Dati menzionati nei file di gestione dei rischi
- I dati menzionati nell'etichettatura e/o nelle IFU (vale a dire vengono affrontati i rischi residui da comunicare all'utente).

La sicurezza clinica è stata dimostrata dai bassi tassi di complicanze individuati nella letteratura clinica peer-reviewed pubblicata, dagli studi clinici sponsorizzati dall'azienda, dalla revisione dei dati post-commercializzazione e dall'assenza di ritiri dal mercato. Non sono stati riscontrati problemi di prestazioni; la letteratura ha esaminato l'uso del FemoSeal™ VCS in questione in conformità con l'uso previsto del fabbricante.

### **1.5 Possibili alternative diagnostiche o terapeutiche**

La compressione manuale viene tradizionalmente utilizzata per ottenere l'emostasi nel sito dell'arteriotomia dopo cateterizzazioni vascolari. È stata associata all'immobilizzazione del paziente per lunghi periodi di tempo (fino a 8 ore dopo una procedura) e a notevoli disturbi e degenze ospedaliere prolungate. Una recente analisi sistematica ha rilevato che il tempo mediano per ottenere l'emostasi con compressione manuale era di 20,8 minuti.<sup>1</sup>

Le alternative alla compressione manuale includono dispositivi emostatici esterni che applicano la compressione meccanica al sito dell'arteriotomia. Questi dispositivi non abbreviano il tempo per l'emostasi o la deambulazione, ma riducono il personale necessario sostituendo la compressione manuale con quella meccanica. I tassi di eventi avversi associati all'uso della compressione meccanica sono simili ai tassi di compressione manuale.

I dispositivi di chiusura vascolare, come FemoSeal™ VCS, sono progettati per chiudere l'arteriotomia. L'obiettivo è ridurre il tempo di emostasi e consentire una deambulazione più rapida. Una recente analisi sistematica, comprendente 13 dispositivi disponibili in commercio, ha rilevato che il tempo mediano per ottenere l'emostasi con un dispositivo di chiusura vascolare era di 5,4 minuti. Il tempo mediano per l'emostasi per i singoli dispositivi di chiusura vascolare variava da 1 minuto (FemoSeal™ VCS) a 14 minuti con la maggior parte dei dispositivi tra 4 e 10 minuti.<sup>1</sup>

Gli eventi avversi comunemente segnalati associati alla chiusura del sito dell'arteriotomia, con compressioni manuali, dispositivi emostatici esterni o dispositivi di chiusura vascolare, comprendono ematoma, emorragia nel sito di accesso, pseudoaneurisma, fistola arterovenosa e infezione. La stessa analisi sistematica (34 studi randomizzati controllati, 14.401 pazienti) ha

rilevato che i tassi di eventi avversi erano simili tra la compressione manuale e l'uso di dispositivi di chiusura vascolare, con l'eccezione che l'emorragia tendeva a essere leggermente più elevata con questi ultimi.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Profilo utente e formazione suggeriti

Gli utilizzatori previsti di FemoSeal™ Vascular Closure System sono medici con una formazione che li abilita a eseguire accessi e chiusure arteriose per procedure endovascolari attraverso l'arteria femorale comune e che hanno partecipato a un programma di formazione per medici FemoSeal™ di Terumo Medical Corporation.

## 1.7 Standard armonizzati e comuni pertinenti

| Riferimento standard | Anno corrente di conformità/Rev. | Descrizione                                                                                                                              |
|----------------------|----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070            | 2014/AMD1:2018                   | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070         | 2014/A1:2018                     | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| Linee guida FDA      | 20 maggio 2021                   | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052           | 2015                             | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213           | 2017                             | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503           | 2020                             | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |

| Riferimento standard | Anno corrente di conformità/Rev. | Descrizione                                                                                                                                                              |
|----------------------|----------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F2182           | 2019                             | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging                                    |
| EN ISO 13485         | 2016/A11:2021                    | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 13485            | 2016                             | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 14644-1          | 2015                             | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1       | 2015                             | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2          | 2015                             | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2       | 2015                             | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3          | 2019                             | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3       | 2019                             | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1          | 2003                             | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1       | 2003                             | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |

| Riferimento standard      | Anno corrente di conformità/Rev. | Descrizione                                                                                                                                   |
|---------------------------|----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14698-2               | 2003/TC1:2004                    | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| EN ISO 14698-2            | 2003/TC 1:2004                   | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| USP < 788>                | Non applicabile                  | PARTICULATE MATTER IN INJECTIONS                                                                                                              |
| Farmacopea europea 2.9.19 | Non applicabile                  | Particulate Contamination: Sub-Visible Particles                                                                                              |
| IEC 62366-1               | 2015                             | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN 62366-1                | 2015                             | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN ISO 14971              | 2019/A11:2021                    | Medical devices — Application of risk management to Medical devices                                                                           |
| ISO 14971                 | 2019                             | Medical devices — Application of risk management to Medical devices                                                                           |
| ASTM F1980                | 2016                             | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                                           |
| EN ISO 10993-1            | 2020                             | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                    |
| ISO 10993-1               | 2018                             | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                    |
| EN ISO 10993-2            | 2006                             | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                                                |
| ISO 10993-2               | 2006                             | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                                                |
| EN ISO 10993-3            | 2014                             | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity                          |



| Riferimento standard | Anno corrente di conformità/Rev. | Descrizione                                                                                                          |
|----------------------|----------------------------------|----------------------------------------------------------------------------------------------------------------------|
| ISO 10993-3          | 2014                             | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4       | 2017                             | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4          | 2017                             | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| EN ISO 10993-5       | 2009                             | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| ISO 10993-5          | 2009                             | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| EN ISO 10993-6       | 2016                             | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |
| ISO 10993-6          | 2016                             | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |
| EN ISO 10993-10      | 2023                             | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                       |
| ISO 10993-10         | 2021                             | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                       |
| EN ISO 10993-11      | 2018                             | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                      |
| ISO 10993-11         | 2017                             | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                      |
| EN ISO 10993-12      | 2021                             | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                       |
| ISO 10993-12         | 2021                             | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                       |
| EN ISO 10993-17      | 2009                             | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances       |



| Riferimento standard | Anno corrente di conformità/Rev. | Descrizione                                                                                                                                                                  |
|----------------------|----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-17         | 2002                             | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                                                               |
| ISO 10993-18         | 2020/A1:2022                     | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-18      | 2020/A1:2022                     | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-23      | 2021                             | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23         | 2021                             | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382           | 2018                             | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756            | 2017                             | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>             | Non applicabile                  | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>            | Non applicabile                  | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72       | 2019                             | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135         | 2014/A1:2019                     | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |

| Riferimento standard | Anno corrente di conformità/Rev. | Descrizione                                                                                                                                                                  |
|----------------------|----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11135            | 2014/A1:2018                     | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7       | 2008/A1:2022                     | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |
| ISO 10993-7          | 2008/A1:2019                     | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                                            |
| EN 556-1             | 2024                             | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices              |
| EN ISO 11737-1       | 2018/A1:2021                     | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                                        |
| ISO 11737-1          | 2018/A1:2021                     | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                                        |
| EN ISO 11138-1       | 2017                             | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                                 |
| ISO 11138-1          | 2017                             | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                                 |
| EN ISO 11138-2       | 2017                             | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                                     |
| ISO 11138-2          | 2017                             | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                                     |
| EN ISO 15223-1       | 2016                             | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                                       |

| Riferimento standard | Anno corrente di conformità/Rev. | Descrizione                                                                                                                             |
|----------------------|----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| ISO 15223-1          | 2016                             | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements  |
| EN 1041              | 2008/A1:2013                     | Information supplied by the manufacturer of medical devices                                                                             |
| EN ISO 11607-1       | 2020/A1:2023                     | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems |
| ISO 11607-1          | 2019/A1:2023                     | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems |
| EN ISO 11607-2       | 2020/A1:2023                     | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes      |
| ISO 11607-2          | 2019/A1:2023                     | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes      |
| ASTM D4169           | 2016                             | Standard Practice for Performance Testing of Shipping Containers and Systems                                                            |
| ASTM F1886/F1886M    | 2016                             | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                     |
| ASTM F2825           | 2018                             | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                |
| ASTM F2096           | [2011 R 2019)                    | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                            |
| ASTM F88/F88M        | 2015                             | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                    |
| MDCG 2021-24         | 2021                             | Guidance on classification of medical devices                                                                                           |

| Riferimento standard | Anno corrente di conformità/Rev. | Descrizione                                                                                                                                                                        |
|----------------------|----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-3          | 2020                             | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD         |
| MDCG 2020-8          | 2020                             | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                                     |
| MDCG 2020-7          | 2020                             | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                                  |
| MDCG 2020-6          | 2020                             | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                               |
| MDCG 2019-9 v1       | 2022                             | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                           |
| MDCG 2019-8 v2       | 2020                             | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices |
| MDCG 2020-15         | 2020                             | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                           |
| MDCG 2021-11         | 2021                             | Guidance on Implant Card – ‘Device types’                                                                                                                                          |
| MDCG 2021-19         | 2021                             | Guidance note integration of the UDI within an organisation’s quality management system                                                                                            |
| MDCG 2018-1 v4       | 2021                             | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                     |
| MDCG 2019-2          | 2019                             | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                 |
| MDCG 2019-1          | 2019                             | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                 |

| Riferimento standard | Anno corrente di conformità/Rev. | Descrizione                                                                                                                                                                                                                                                   |
|----------------------|----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2018-7          | 2018                             | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6          | 2018                             | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |
| MDCG 2018-4          | 2018                             | MDCG 2018-4 Annex: UDI database Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                                                                                                  |
| MDCG 2018-3 v1       | 2020                             | Guidance on UDI for systems and procedure packs                                                                                                                                                                                                               |
| MDCG 2021-25         | 2021                             | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC                                                                 |
| MEDDEV 2.12-2 Rev 2  | 2012                             | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                                                                                        |

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### 3.0 CRONOLOGIA DELLE REVISIONI

| Numero di revisione<br>SSCP   | Data di rilascio | Descrizione delle<br>modifiche                                                            | Revisione convalidata<br>dall'Organismo notificato                                                                                                                                                                                                                                                                                                                                |
|-------------------------------|------------------|-------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022                  | 20 gennaio 2023  | Prima edizione, previa<br>certificazione MDR CE                                           | <p><input checked="" type="checkbox"/> Sì</p> <p>Lingua di convalida: English</p> <p><input type="checkbox"/> No (applicabile solo per<br/>dispositivi impiantabili di classe<br/>IIa o alcuni dispositivi IIb<br/>(MDR, articolo 52 (4), 2°<br/>paragrafo) per i quali l'SSCP<br/>non è ancora convalidato<br/>dall'ON)</p> <p><input type="checkbox"/> Altro (specificare):</p> |
| SSCP-FS-2023 -<br>Revisione 1 | 15 marzo 2024    | Aggiornato per il<br>periodo compreso tra il<br>1° gennaio 2019 e il<br>31 dicembre 2023. | <p><input checked="" type="checkbox"/> Sì</p> <p>Lingua di convalida: English</p> <p><input type="checkbox"/> No (applicabile solo per<br/>dispositivi impiantabili di classe<br/>IIa o alcuni dispositivi IIb<br/>(MDR, articolo 52 (4), 2°<br/>paragrafo) per i quali l'SSCP<br/>non è ancora convalidato<br/>dall'ON)</p> <p><input type="checkbox"/> Altro (specificare):</p> |
| SSCP-FS-2024<br>Revisione 1   |                  | Aggiornato per il<br>periodo compreso tra il<br>1° settembre 2019 e il<br>31 agosto 2024. | <p><input type="checkbox"/> Sì</p> <p>Lingua di convalida: English</p> <p><input type="checkbox"/> No (applicabile solo per<br/>dispositivi impiantabili di classe<br/>IIa o alcuni dispositivi IIb<br/>(MDR, articolo 52 (4), 2°<br/>paragrafo) per i quali l'SSCP<br/>non è ancora convalidato<br/>dall'ON)</p> <p><input type="checkbox"/> Altro (specificare):</p>            |

|                             |               |                                                            |                                                                                                                                                                                                                                                                                                                                                                  |
|-----------------------------|---------------|------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>Revisione 2 | June 20, 2025 | Revisionato in base alle<br>query NSAI per la<br>convalida | <input checked="" type="checkbox"/> Sì<br>Lingua di convalida: English<br><br><input type="checkbox"/> No (applicabile solo per<br>dispositivi impiantabili di classe<br>IIa o alcuni dispositivi IIb<br>(MDR, articolo 52 (4), 2°<br>paragrafo) per i quali l'SSCP<br>non è ancora convalidato<br>dall'ON)<br><br><input type="checkbox"/> Altro (specificare): |
|-----------------------------|---------------|------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

안전성 및 임상 성과 요약

**FemoSeal™ Vascular Closure System**

|                                |                                                                                              |
|--------------------------------|----------------------------------------------------------------------------------------------|
| 제조사                            | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 USA          |
| 제조사 SRN                        | US-MF-000019594                                                                              |
| Management Representative/PRRC | Kimberly Feitl<br>Vice President, Quality                                                    |
| 기본 UDI-DI                      | 38970FS79                                                                                    |
| EMDN 번호                        | C900199 – 지혈 장치-기타                                                                           |
| 장치 등급                          | 3등급                                                                                          |
| CE 마크 첫 부착 연도                  | 2005                                                                                         |
| EU Representative              | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgium<br>SRN: BE-AR-000001433 |
| 통지 기관                          | NSAI<br>CE 0050                                                                              |

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안전성 및 임상 성과 요약(SSCP)은 FemoSeal™의 혈관 봉합기구(VCS) 안전성 및 임상 성과의 주요 측면에 대한 업데이트 요약을 공개합니다.

사용자/의료 전문가를 위한 기기의 안전성 및 임상 성능에 대한 요약은 아래 **섹션 1.0**에 제공됩니다.

## 1.0 사용자/의료 전문가를 위한 요약

SSCP는 장치의 안전한 사용을 보장하기 위해 주요 문서로 사용 지침을 대체하지 않으며, 대상이 되는 사용자 또는 환자에게 진단 또는 치료 제안을 하기 위한 것이 아닙니다. SSCP는 이식 카드 또는 기타 필수 문서의 필수 정보를 대체하기 위한 것이 아닙니다.

### 1.1 기기 사용 목적

#### 1.1.1 사용 목적

FemoSeal™ 혈관 봉합기구는 총 대퇴 동맥을 통한 경피적 카테터 삽입 후 동맥 천자를 봉합하기 위한 의료기기입니다.

#### 1.1.2 적응증

FemoSeal™ 혈관 봉합기구는 7F(2.33mm) 이하의 시술용 도관을 사용하여 경피적 카테터 삽입을 받은 환자의 일반적인 대퇴 동맥 천자(동맥 절개술)를 봉합하는 데 사용됩니다.

#### 1.1.3 금기 사항 및/또는 제한 사항

FemoSeal™ 혈관 봉합기구는 7F(2.33mm) 이상의 도관 또는 장치를 사용한 동맥 절개술 환자에게는 사용할 수 없습니다.

#### 1.1.4 표적 환자 집단

FemoSeal™ 혈관 봉합기구의 안전성과 유효성이 7F(2.33mm) 이하의 시술용 도관을 사용하여 경피적 카테터 삽입을 받은 18세 이상의 환자에서 확인되었습니다.

#### 1.1.5 특수 환자 집단

다음 환자 집단에서 FemoSeal™ 혈관 봉합기구의 안전성과 유효성은 확인되지 않았습니다.

- 기존 자가 면역 질환이 있는 환자.
- 치료용 혈전 용해제를 복용하는 환자.
- 임상적으로 중대한 말초 혈관 질환이 있는 환자.
- 비 조절성 고혈압 (> 수축기 220mmHg 또는 > 이완기 110mmHg)이 있는 환자.
- 혈소판 감소증(< 100,000 혈소판 수치) 또는 빈혈(Hgb < 10 mg/dl)을 포함한 출혈 장애가 있는 환자.

- 총 대퇴 동맥 내강이 5mm 미만인 환자.
- 신장 및/또는 간 장애 환자.
- 기타 관련된 동반이환 환자.
- 특정 인종 및/또는 민족 출신 집단.
- 72시간 이내에 심근 경색이 있었던 환자.
- 천자 부위에 혈관 이식 또는 스텐트가 있는 환자.
- 임신 중이거나 수유 중인 환자.
- 18세 미만의 환자.

### 1.1.6 대상 사용자

FemoSeal™ 혈관 봉합기구의 대상 사용자는 총 대퇴 동맥을 통한 혈관 내 시술에 대한 동맥 접근 및 지혈 수행 자격을 갖추었으며 테루모 메디컬 주식회사(Terumo Medical Corporation) FemoSeal™ 의사 교육 프로그램에 참여한 의사입니다.

## 1.2 장치 설명

### 1.2.1 장치 설명

FemoSeal™ 테루모 메디컬 주식회사(Terumo Medical Corporation, TMC)가 제작한 혈관 봉합기구는 총 대퇴 동맥을 통한 경피적 카테터 삽입 후 대퇴 동맥 지혈을 하도록 만들어진 재흡수 가능한 혈관 봉합기구입니다.

FemoSeal™ 봉합 부품은 2개의 재흡수성 폴리머 디스크, 내부 씰(seal) 및 외부 잠금 디스크로 구성되어 있으며, 이는 재흡수성 멀티 필라멘트에 의해 결합되며 기계적으로 동맥 절개를 봉합합니다(그림 1.1 및 그림 1.2 참조). 콘 하우징 도관을 통해 배치된 후, 외부 잠금 디스크가 멀티 필라멘트 샤프트에 탬핑되어 내부 잠금 디스크와 외부 잠금 디스크 사이의 천자 부위가 기계적으로 봉합됩니다. 내부 씰(seal)과 외부 잠금 디스크는 멀티 필라멘트 샤프트의 마찰을 통해 제 위치에 고정됩니다. 기계적 수단에 의해 지혈됩니다. 봉합 부품은 가수분해에 의해 분해됩니다.

삽입형 봉합 부품, 내부 씰(seal) 및 외부 잠금 디스크는 18개월 후에 분해되며 멀티 필라멘트는 2년에서 3년 후 주변 조직에 의한 가수분해로 분해 및 흡수됩니다. 동맥 절개술에서 압박을 유지하기 위한 삽입형 봉합 부품의 기능은 최대 8시간 동안 시험되었습니다. 분해 생성물은 대사 작용을 거친 후 소변으로 배설되거나 폐를 통해

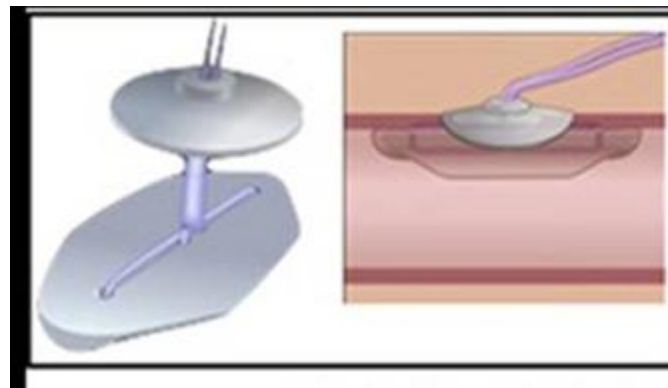


이산화탄소로 배출됩니다. 동물 연구에서 축적 효과가 관찰되지 않았습니다. 시술 중 살아있는 조직이나 혈액과 접촉하게 되는 FemoSeal™의 추가 구성 요소에는 콘 하우스링 도관, 확장기, 탬핑 튜브, 푸셔 및 가이드와이어가 있습니다.

그림 1.1 각각 내부 썰 및 외부 잠금 디스크

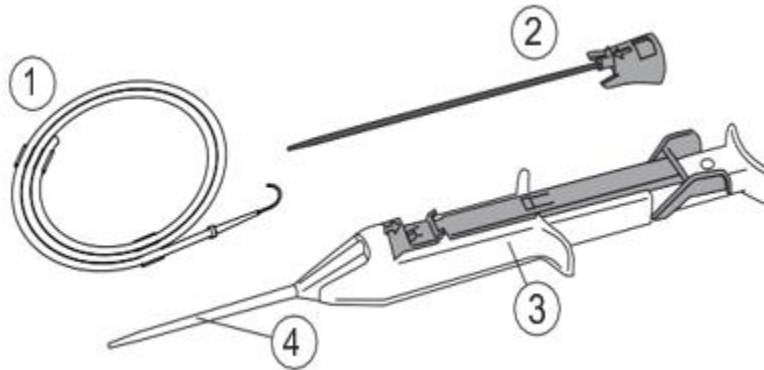


그림 1.2 내부 썰 및 외부 잠금 디스크 배치



FemoSeal™ 장치에는 확장기 및 0.038(0.97mm) OD, 27.5"(70cm) 길이의 가이드와이어 및 J-스트레이트너가 함께 포장됩니다. 아래 그림 1.3을 참조하십시오. 가이드와이어는 폴리에틸렌 튜브 내에 포함됩니다. 모든 구성품은 고정된 종이 트레이에 포장됩니다. 포장에는 환자 이식 카드도 포함됩니다. FemoSeal™ 혈관 봉합기구는 장치가 의도한 대로 기능하는 데 추가 부속품을 필요로 하지 않으며 본 장치는 제품 포장 안에 들어 있는 확장기 및 가이드와이어와 함께 사용해야 합니다.

그림 1.3 가이드와이어와 확장기가 장착된 FemoSeal™ VCS 장치



### 1.2.2 원자재 및 구성품

아래 표 1.1은 FemoSeal™ VCS의 구성품을 나열합니다.

표 1.1 FemoSeal™ VCS 원자재 및 구성품

| 구성품<br>번호 | 설명                                            | 재료                                                                                                                   |
|-----------|-----------------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| 1         | 가이드와이어 J-스트레이트너를<br>포함한 0.038"(0.97mm) 가이드와이어 | 가이드와이어: 304 스테인레스<br>스틸<br><br>J 스트레이트너: 폴리프로필렌,<br>자주색 안료<br><br>클립: 폴리에틸렌<br><br>튜브: 폴리에틸렌                         |
| 2         | FemoSeal 확장기                                  | 허브: 테트라히드로푸란, 청색<br>안료, 폴리부틸렌<br>텔레프탈레이트(PBT)<br><br>튜브: 고밀도 폴리에틸렌(HDPE),<br>검정 안료<br><br>윤활제: 실리콘 Dow Corning 360   |
| 3/4       | FemoSeal 장치                                   | 성형된 RD7 -<br>내부 씬(seal) 및<br>외부 잠금<br>디스크*<br><br>글리콜라이드, 트리메틸렌<br>카보네이트, ε-카프로락톤 및 TMP<br>간 공중 합체:<br>트리메틸올프로판(개시제) |

|  |  |           |                                                                                                            |
|--|--|-----------|------------------------------------------------------------------------------------------------------------|
|  |  | 멀티 필라멘트 * | L, L-락티드, 트리메틸렌 카보네이트, ε-카프로락톤, 및 1,3 프로판디올(개시제) 간의 분절 공중합체<br><br>코팅은 글리콜라이드, ε-카프로락톤 및 L-라이신 간의 공중합체입니다. |
|  |  | 템핑 튜브     | 폴리프로필렌                                                                                                     |
|  |  | 푸셔        | 304V 스테인레스 스틸                                                                                              |
|  |  | 슬라이더      | 폴리부틸렌 테레프탈레이트(PBT)                                                                                         |
|  |  | 하우징       | 폴리부틸렌 테레프탈레이트(PBT)                                                                                         |
|  |  | 버튼        | 폴리부틸렌 테레프탈레이트(PBT)                                                                                         |
|  |  | 버튼 리드     | 폴리옥시메틸렌(POM)/폴리아세탈 공중합체                                                                                    |
|  |  | 슬리브       | 폴리부틸렌 테레프탈레이트(PBT)                                                                                         |
|  |  | 스페이서      | 폴리부틸렌 테레프탈레이트(PBT)                                                                                         |
|  |  | 콘         | 폴리프로필렌                                                                                                     |
|  |  | 하우징 리드    | 폴리부틸렌 테레프탈레이트(PBT)                                                                                         |
|  |  | 안전 장치     | 폴리부틸렌 테레프탈레이트(PBT), 청색 안료                                                                                  |
|  |  | 슬리브 리드    | 폴리부틸렌 테레프탈레이트(PBT)                                                                                         |
|  |  | 튜브 개스킷    | 실리콘 쇼어(경도) A 70                                                                                            |
|  |  | 하우징 개스킷   | 실리콘 쇼어 A 50                                                                                                |
|  |  | 스프링       | 302 스테인레스 스틸                                                                                               |
|  |  | 콘 하우징 도관  | 폴리프로필렌<br>실리콘 Dow Corning 360, 핵산                                                                          |

\* 삽입형 장치의 일부; 삽입형 구성품은 MRI에 안전합니다

FemoSeal™ VCS는 에틸렌 옥사이드(EO)로 멸균 처리되었으며 일회용 의료 기기입니다.  
FemoSeal™ VCS 장치는 재사용할 수 없도록 만들어졌습니다.

## 작동 모드

FemoSeal™ VCS는 총 대퇴 동맥 내외부에 삽입형 봉합 부품을 배치하여 기계적 지혈을 촉진합니다. 천공 부위를 지혈하는 내부 씰(seal)과 내부 씰(seal)을 제 위치에 고정하는 외부 잠금 디스크가 출혈을 방지하는 메커니즘을 제공합니다.

### 1.2.3 임상적 유익성

FemoSeal™ VCS는 총 대퇴 동맥 천자 후 혈관 봉합과 관련하여 다음과 같은 임상적 유익성을 제공합니다.

- 지혈까지 시간 단축<sup>1</sup>
- 조기 활동까지 시간 단축<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

### 1.2.4 이전 세대 혹은 변형 모델

- FemoSeal™ VCS (#11200)의 첫 번째 버전은 2005년 및 2006년 일정 기간 유럽 시장에서 판매되었습니다.
- 현재 FemoSeal™ VCS(#11202)는 2006년 3월 28일 이후 전달 시스템 개선을 포함하여 출시되었습니다.

### 1.2.5 기기와 함께 사용하도록 고안된 부속품

FemoSeal™ 장치는 확장기, 0.038"(0.97 mm) OD, 27.5"(70 cm) 길이의 가이드와이어 및 J-스트레이트너와 함께 포장됩니다. 가이드와이어는 FemoSeal™ 장치의 부속품입니다. J-스트레이트너는 가이드와이어의 구성 요소이며, 확장기는 FemoSeal™ 장치의 구성 요소입니다. 가이드와이어만 부속품으로 간주됩니다. 가이드와이어는 폴리에틸렌 튜브 내에 포함됩니다. 모든 구성품은 고정된 종이 트레이에 포장됩니다. 포장에는 환자 이식 카드도 포함됩니다. FemoSeal™ 혈관 봉합기구는 장치가 의도한 대로 기능하는 데 추가 부속품을 필요로 하지 않으며 본 장치는 제품 포장 안에 들어 있는 확장기 및 가이드와이어와 함께 사용해야 합니다.

### 1.2.6 기기와 함께 사용하도록 고안된 기타 기기 및 제품

FemoSeal™ VCS는 제대로 작동하기 위해 추가 장치가 필요하지 않습니다.

### 1.3 위험 및 경고

#### 1.3.1 잔존 위험 및 바람직하지 않은 영향

잔여 위험의 결과로 FemoSeal™ VCS를 사용하는 것과 관련된 알려진 또는 예측 가능한 이상 사례, 피해 및 합병증은 표 1.2에 나와 있습니다. 발생률은 위험 문서 분석을 기반으로 하며, 2019년 9월 1일부터 2024년 8월 31일까지의 시판 후 조사 데이터를 기반으로 계산됩니다. FemoSeal™ VCS에 대해 알려지지 않은 잔존 위험성이 없으며 모든 해당 위험은 사용 지침 및 위험 관리 프로세스를 통해 해결했습니다.

표 1.2. FemoSeal 이상 사례/합병증

| 피해      | 발생률(%) | 완화 조치                                                               |
|---------|--------|---------------------------------------------------------------------|
| 알레르기 반응 | 0.0000 | 가능한 한 위험을 줄이기 위한 조치와 계획은 제품 설계 특징, 제조 지침, 제품 라벨링 및 의사 교육으로 해결되었습니다. |
| 동맥류     | 0.0000 |                                                                     |
| AV 누관   | 0.0001 |                                                                     |
| 실혈/출혈   | 0.0280 |                                                                     |
| 사망      | 0.0002 |                                                                     |
| 반상 출혈   | 0.0000 |                                                                     |
| 색전증     | 0.0000 |                                                                     |
| 이물질 반응  | 0.0000 |                                                                     |
| 혈종      | 0.0027 |                                                                     |
| 출혈      | 0.0001 |                                                                     |
| 감염 증상   | 0.0002 |                                                                     |
| 염증성 반응  | 0.0000 |                                                                     |
| 마비      | 0.0000 |                                                                     |
| 통증      | 0.0000 |                                                                     |
| 환자 불편감  | 0.0004 |                                                                     |
| 시술 지연   | 0.0065 |                                                                     |
| 가성 동맥류  | 0.0004 |                                                                     |
| 후복막 출혈  | 0.0002 |                                                                     |

| 피해            | 발생률(%) | 완화 조치 |
|---------------|--------|-------|
| 패혈증           | 0.0000 |       |
| 혈전 색전증        | 0.0000 |       |
| 혈전증           | 0.0001 |       |
| 혈관 폐색증/하지 허혈증 | 0.0002 |       |
| 혈관 천공         | 0.0000 |       |
| 혈관 조직 절개/자상   | 0.0003 |       |

### 1.3.2 경고 및 주의 사항

#### 경고 사항

1. 포장에 손상이 있거나 멸균 장벽이 손상된 경우 사용하지 마십시오.
2. 유효기간이 지난 후에는 사용하지 마십시오. 생분해성 구성품이 제대로 기능하지 않을 수 있습니다.
3. 어떤 품목이라도 손상되거나 결함이 보이면 사용하지 마십시오.
4. 시술용 도관 또는 주변 조직에 세균 오염이 발생한 경우 FemoSeal™ 혈관 봉합기구를 사용하면 감염이 발생할 수 있습니다.
5. 후방 동맥벽이 뚫렸거나 두 개 이상의 동맥이 뚫렸다고 의심되는 경우 FemoSeal™ 혈관 봉합기구에만 의존하여 동맥을 지혈하지 마십시오. 추가적으로 수동 압박법이나 기계적 압박법을 사용하십시오.
6. 천공 부위가 대퇴 동맥의 분기부에 있거나 원위부에 있는 경우 내측 씰(seal)이 잘못 배치될 위험이 있으므로 FemoSeal™ 혈관 봉합기구를 사용해서는 안 됩니다. 이는 출혈 합병증 및/또는 정상 혈류 장애를 유발할 수 있습니다.
7. 절개 부위에서 동맥 출혈이 지속되는 경우 지혈되기 전까지 멀티 필라멘트를 자르지 마십시오. 지혈이 되지 않으면 멸균 상처 드레싱으로 멀티 필라멘트를 고정하고 지혈될 때까지 보조 압박을 가하십시오. 동맥 출혈이 지속되는 경우, 심각한 출혈 합병증이 발생하여 환자 상해 또는 사망을 초래할 수 있습니다.
8. 천자 부위가 서혜부 인대에 근접한 경우에는 후복막 혈종이 생길 수 있으므로 FemoSeal™ 혈관 봉합기구를 사용하지 마십시오.
9. 출혈 위험이 큰 환자는 혈액 손실이 증가하여 수혈이 필요할 수 있습니다.

10. 내부 디스크가 분리되면 혈전 및/또는 색전 현상을 일으킬 수 있습니다.

### 주의 사항

1. FemoSeal™ 혈관 봉합기구 배치 시술은 장치 사용에 대한 적절한 교육을 받은 의사가 수행해야 합니다.
2. FemoSeal™ 혈관 봉합기구를 배치하기 전에 제한된 대퇴 혈관 조영술 또는 초음파 유도식 대퇴부 천자를 실시하십시오.
3. 다음의 경우 시술을 중단합니다.
  - 총 대퇴 동맥의 내강 직경이 < 5mm인 경우.
  - 협착증 및/또는 총 대퇴 동맥 천자 부위 근처에 상당한 플라크가 있는 경우.
  - 동맥 천자 부위가 대퇴 동맥 분기점 또는 대퇴 동맥 분기점의 말단에 있는 경우.
  - 일반적인 대퇴 동맥 천자 부위 근처에 비정상적인 분지 또는 혈관 이상이 있는 경우.
4. 혈종이 있는 경우, 콘 하우징 도관을 동맥에 올바르게 삽입하기 위해 각별히 주의해야 합니다.
5. 단일벽 천자 기법을 사용하십시오. 동맥의 후벽을 뚫지 마십시오.
6. FemoSeal™ 혈관 봉합기구를 사용할 때는 항상 멸균법을 준수하십시오.
7. FemoSeal™ 혈관 봉합기구는 일회용이며 어떤 방식으로든 재멸균 또는 재사용해서는 안 됩니다. FemoSeal™ 장치는 재사용할 수 없도록 만들어졌습니다.
8. 내부 씰(seal) 배치 시 예상치 못한 저항이 발생하면 시술을 중단하십시오.
9. 내부 씰(seal)을 올바르게 배치하려면 엄지손가락 위치를 조정하여 버튼이 뒤로 자유롭게 튀어 오를 수 있도록 합니다.
10. 외부 잠금 디스크를 배치하기 전에 FemoSeal™ 장치의 콘 하우징 도관의 팁이 피부 표면 아래에 있는지 확인하십시오. 외부 잠금 디스크는 대퇴 동맥과 피부 사이의 거리가 짧은 환자의 피부 표면 위에 부주의하게 배치될 수 있습니다.
11. 올바른 배치를 위해 배치 전에 피부 절개가 필요할 수 있습니다.
12. 내부 씰(seal)이 동맥 내부에 있지만 버튼을 완전히 누르고 외부 잠금 디스크를 배치할 수 없는 경우 FemoSeal™ 봉합 부품을 제거하기 위해 수술이 필요할 수 있습니다.

13. 18개월 이내에 동일한 대퇴 동맥의 재천자가 필요할 경우, 이전의 FemoSeal™ 혈관 봉합기구 접근 부위에 적어도 1센티미터 이상 근접하도록 천자를 해야 합니다.
14. 봉합 부위 검사와 관련하여 의사의 지시를 따르도록 환자에게 알려주십시오.
15. 환자에게 향후 18개월간 환자 정보 카드를 소지하도록 지시하십시오

### 퇴원 시 주의 사항

퇴원을 고려하기 전에 환자의 임상 상태에 대해 다음과 같은 내용을 평가하십시오.

1. 봉합 부위에 출혈 및/또는 혈종.
2. 걷는 동안 통증.
3. 봉합 부위의 감염 징후.

### 1.3.3 현장 안전 시정 조치

2019년 9월 1일부터 2024년 8월 31일까지 FemoSeal™ VCS와 관련된 현장 안전 시정 조치가 1건 있었습니다.

2022년, Terumo는 Elkton에서 제조한 FemoSeal 제품의 탬핑력 측정 및 견인력에 대한 공정 및 로트 릴리스 테스트 실패를 주장하는 컴플레인으로 인해 자발적으로 FemoSeal™ VCS를 리콜했습니다. 한국에서 총 950개가 리콜되었습니다.

## 1.4 임상 평가 및 시판 후 임상 추적관찰

**Table 1.3**에는 FemoSeal™ VCS의 출시와 더불어 시판 후 연구 및 시판 후 임상 추적 활동을 포함하는 핵심 연구 목록이 나열되어 있습니다. 연구에 사용된 장치의 버전은 아래 표에 나와 있습니다. 첫 번째 버전의 FemoSeal™ VCS(#11200)는 2006년까지 시장에 출시되었으며, 다음 버전(#C11202)은 2006년에 시장에 출시되어 현재까지 시장에서 판매되고 있습니다.

**표 1.3 핵심 연구 요약**

| 시판 전 기능성 동물 실험                                                                                                                                                                                                                                                          | 장치 버전 |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200 |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200 |



|                                                                                                                                                                                                                                                                 |                   |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France). | 11200             |
| 최초의 사람 대상 임상 시험                                                                                                                                                                                                                                                 |                   |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                    | 11200             |
| 시판 후 임상 연구 완료                                                                                                                                                                                                                                                   |                   |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                                                                      | C11202<br>(현재 장치) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                                                                               | C11202<br>(현재 장치) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                                                                                                                                                  | C11202<br>(현재 장치) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)                                                                                                                                          | C11202<br>(현재 장치) |
| 계획/진행 중인 시판 후 임상시험                                                                                                                                                                                                                                              |                   |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                                                                                                                                                      | C11202<br>(현재 장치) |
| 시판 후 임상 추적관찰 활동                                                                                                                                                                                                                                                 |                   |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                                                                                                                                                       | C11202<br>(현재 장치) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                                                                                                                                                              | C11202<br>(현재 장치) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024)                                                                                                                                 | C11202<br>(현재 장치) |

#### 1.4.1 시판 전 데이터 요약(동물 시험 및 임상 연구)

아래 표 1.4는 동물 시험 및 임상 연구의 모든 시판 전 연구를 기술합니다.

표 1.4 시판 전 연구 요약

| 시판 전 기능성 동물 실험                                                                                                             |                                |                  |                                                                  |                                                                           |                                                                                  |
|----------------------------------------------------------------------------------------------------------------------------|--------------------------------|------------------|------------------------------------------------------------------|---------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| 연구 이름                                                                                                                      | 연도/CI                          | 연구 유형            | 연구 목표                                                            | 주요 단계                                                                     | 잠재적인 허용 기준                                                                       |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional | 2000<br>Radi Medical System AB | 동물 연구;<br>탐색적 조사 | 이 연구의 목적은 혈관계에서 지혈하도록 설계된 생분해성 임플란트의 생체 적합성 및 생체 기능성을 평가하는 것입니다. | N= 성체 암컷 양 3마리, 시점 당 동물 1마리<br><br>조직병리학적 분석, 육안 등급 지정 및 초미세 구조 분석에 대한 추적 | 동맥 개방성<br>• 배치 후 혈류 평가 - 시술에 기인한 임시 동맥 혈관 경련과 관련된 2/3 혈류 감소, 두 가지 모두 좌측 경동맥에서 발생 |

|                                                                                                                                           |                    |  |                                            |                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-------------------------------------------------------------------------------------------------------------------------------------------|--------------------|--|--------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 프랑스 Biomatech에서 수행 |  | 보고서는 연구 번호 862(문서 번호 1051-01)의 예비 동물을 다룹니다 | <ul style="list-style-type: none"> <li>12개월</li> <li>15개월</li> <li>18개월</li> </ul> <p>색조 도플러 초음파 추적 - 경동맥과 대퇴 동맥 부위에서 30일 간</p> | <ul style="list-style-type: none"> <li>색조 도플러 초음파 검사(4주) - 3/3(100%), 이식 후 30일 내 주요 혈류량 감소 없음</li> </ul> <p>육안 관찰</p> <ul style="list-style-type: none"> <li>12개월 - 해부학적으로 보이는 폐색이 없으므로 개방성이 육안으로 확인됨; 육안상 국소 불내성 병변(출혈, 괴사 또는 신혈관 형성) 없음; 내부 디스크의 피막화가 표시됨</li> <li>15개월 - 육안상 관찰로는 염증 징후가 없음; 내부 또는 외부 디스크의 잔여물이 확인되지 않음; 외부 디스크의 영역에 있는 피막 조직은 12개월간 관찰한 것과 동일하게 나타남</li> <li>18개월 - 육안상 관찰로는 국소 불내성의 징후가 없었고, 외부 디스크가 보였으며(3/3건), 내부 디스크가 완전히 분해됨; 1/3(왼쪽 총경동맥) - 이식 부위에서 관찰된 동맥벽의 함몰(장치 배치와 관련이 있을 수 있음)</li> </ul> <p>결론</p> <ul style="list-style-type: none"> <li>육안상으로, 이식 후 12개월, 15개월 및 18개월에, 괴사성, 퇴행성, 또는 혈전성 징후가 발견되지 않았습니다.</li> <li>내부 및 외부 디스크의 분해 과정은 12개월에서 18개월 사이에 진행되는 것으로 보였고, 약간 백색의 조직이 이식된 부위를 덮으며 18개월에 완전히 완료되었습니다.</li> <li>조직학적으로, 18개월 후 고분자 물질은 더 이상 가시적이지 않았지만, 관내 섬유</li> </ul> |
|-------------------------------------------------------------------------------------------------------------------------------------------|--------------------|--|--------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                                                                                                                                                                                                                                                                         |                                                       |               |                                                         |                                                                                                                                                                                                               | 조직이 존재했습니다.<br>괴사성, 퇴행성 또는<br>혈전성 병변은<br>나타나지 않았습니다.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|---------------|---------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 2002 Radi Medical System AB<br><br>프랑스 Biomatech에서 수행 | 동물 연구; 탐색적 조사 | 이 연구의 목적은 혈관계에서 지혈하도록 설계된 생분해성 임플란트의 생체 적합성을 평가하는 것입니다. | 추적관찰(이식 후)<br><ul style="list-style-type: none"><li>• 12주</li><li>• 24주</li><li>• 36주</li></ul><br>N = 양 12마리, 시점당 3마리, 12개월, 15개월 및 18개월에 예비 동물 3마리 해부<br><br>이식 부위 - 좌우 대퇴 동맥, 좌우 총경동맥<br><br>색조 도플러 초음파 분석 | <u>4주 후 경동맥 및 대퇴 동맥의 개방성</u><br><ul style="list-style-type: none"><li>• 주 혈류량 감소 0/12(0%)</li></ul><br><u>주 혈류량 감소 없음</u><br><ul style="list-style-type: none"><li>• 장치 삽입과 관련된 심각한 혈류 장애 0/12(0%)</li><li>• 일시적인 동맥혈관 경련으로 인해 좌측 총경동맥 2/12(16.6%)의 혈류 감소(장치가 아닌 수술에서 기인함)</li></ul><br><u>추적관찰 시 혈류 장애</u><br>12주 - 0/12(0%)<br>24주 - 0/12(0%)<br>36주 - 0/12(0%)<br><br>혈압 측정(양 3마리 - 36주)<br><ul style="list-style-type: none"><li>• 주 혈류 감소가 발견되지 않음</li></ul><br><br>통합 및 분해를 위한 거시적 데이터(0~4등급)<br><br><u>경동맥 부위</u><br><u>내측</u><br>-피막 형성<br>12주 1.3<br>24주 0.8<br>36주 0.7<br>-물질 분해<br>12주 2.2<br>24주 2.3<br>36주 0.7<br><u>외측</u><br>-피막 형성<br>12주 2.0<br>24주 1.0<br>36주 0.8 |

|  |  |  |  |  | -물질 분해<br>12주 2.0<br>24주 2.7<br>36주 3.2<br><br><u>대퇴 동맥 부위</u><br>외측<br>-피막 형성<br>12주 1.0<br>24주 2.7<br>36주 1.0<br>-물질 분해<br>12주 2.0<br>24주 2.4<br>36주 3.0<br><br>내측<br>-피막 형성<br>12주 2.0<br>24주 1.2<br>36주 1.0<br>-물질 분해<br>12주 1.0<br>24주 2.2<br>36주 3.0<br><br><u>통합, 분해 및 염증성 변수에<br/>         대한 조직학적 데이터(관련<br/>         값의 평균, 색인 0~4) n=6</u><br><br><u>경동맥 부위</u><br>외측 섬유증<br>12주 - 2.3<br>24주 - 2.3<br>36주 - 1.8<br>내측 신생혈관내막<br>12주 - 3.0<br>24주 - 2.7<br>36주 - 3.3<br>물질 분해<br>12주 - 1.7<br>24주 - 3.0<br>36주 - 3 +<br>염증 매개 변수(대식 세포)<br>12주 - 3.0<br>24주 - 1.7 |
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|  |  |  |  |  | 36주 - 1.7<br><u>대퇴 동맥 부위</u><br>외측 섬유증<br>12주 - 1.3<br>24주 - 1.5<br>36주 - 1.7<br>내측 신생혈관내막<br>12주 - 3.7<br>24주 - 3.3<br>36주 - 3.8<br>물질 분해<br>12주 - 2.0<br>24주 - 3.0<br>36주 - 3+<br>염증 매개 변수(대식 세포)<br>12주 - 3.5<br>24주 - 1.8<br>36주 - 1.8<br><br><u>조직 형태학적 개방성 값</u><br>경동맥 부위<br>12주 74.0%<br>24주 81.9%<br>36주 - 89.43%<br>대퇴 동맥 부위<br>12주 - 42.2%<br>24주 - 73.21%<br>36주 - 78.71%<br><br><u>미국 혈관 개방성(평균 %)</u><br>경동맥 부위<br>12주 94.6%<br>24주 - 96.7%<br>36주 - 94.7%<br>대퇴 동맥 부위<br>12주 - 66.9%<br>24주 - 63.6%<br>36주 - 75.1%<br><br>결론<br><ul style="list-style-type: none"> <li>12주, 24주, 또는 36주에 유의미한 국소 불내성 징후가 발견되지 않았습니다(눈에 보이는 염증성, 괴사성,</li> </ul> |
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|                                                                                                                                                                                                                                                                        |                                                                                  |              |                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                        |
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|                                                                                                                                                                                                                                                                        |                                                                                  |              |                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                 | <p>또는 퇴행성 병변의 부재)</p> <ul style="list-style-type: none"> <li>• 숙주 및 장치와 관련하여 기록된 유의미한 조직 이상 반응 없음</li> <li>• 임플란트 분해는 36주에 거의 완료되었습니다</li> </ul>                                                                                                                                                                                                                                                                                       |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002<br/><br/>Radi Medical System AB<br/><br/>프랑스<br/><br/>Biomatech에서 수행</p> | <p>동물 연구</p> | <p>이 연구의 목적은 혈관계에서 지혈하도록 설계된 생분해성 임플란트의 생체 적합성 및 생체 기능성을 평가하는 것입니다. 실험된 장치는 지혈을 위해 동맥 내 천자 구멍 내에 들어가도록 되어 있습니다. 한 디스크는 동맥의 천자 구멍에 들어가고 다른 디스크는 동맥 외부에서 내부 디스크를 조여줍니다. 두 디스크는 유도관을 통해 삽입했습니다. 디스크는 출혈을 방지하고, 혈관 벽을 매우며, 최종적으로 분해되어 흡수되도록 제작되었습니다. 본 연구는 양과 돼지의 기능성 이식 후 데이터를 수집하고 분석하여 순환계에서 사용할 때 생리적 기능을 유지할 수 있는 임플란트의 기능을 평가하고 숙주 및 장치의 반응(물리적 무결성, 해부 시 조직의 피막 형성)을 파악하며 임플란트의 분해를 평가하기 위해 설계되었습니다.</p> | <p>이식 기간/추적 관찰은 모든 동물에 대해 5주입니다</p> <p>양 4마리, 돼지 1마리</p> <p>14개의 봉합 부품</p> <p>양 2마리에 봉합 부품 8개 이식,</p> <p>돼지 1마리에 봉합 부품 2개 이식</p> <p>두 개의 봉합 부품을 동일한 대퇴 동맥에 이식했을 때, 부품이 이식된 거리는 &gt;30mm입니다.</p> | <p>이식 직후 기준(염증, 괴사, 출혈 또는 기타 병변) 또는 얇은 가성 내막층 형성이 보고되었습니다. 내부 디스크 피막 형성에 특히 중점을 두면서, 장치의 초기 조직 통합에 집중했습니다.</p> <p>육안상으로 국소 불내성 또는 혈전 형성의 유의미한 징후가 관찰되지 않았습니다. 육안상으로 대퇴 동맥 내에 봉합 부품을 이식한 후 양과 돼지 사이의 어떠한 차이도 나타나지 않았습니다. 육안상으로 국소 불내성 또는 혈전 형성의 유의미한 징후가 관찰되지 않았습니다. 육안상으로 대퇴 동맥 내에 봉합 부품을 이식한 후 양과 돼지 사이의 어떠한 차이도 나타나지 않았습니다.</p> <p>양 내에 이식한 부위에 대한 조직학적 분석에 따르면 국소 부작용은 나타나지 않았습니다. 내부 및 외부 디스크는 분해되는 조직을 보였으며 일부 경우에는 더 작은 부분으로</p> |

|                                                                                                                                                       |                              |                    |                                                                                                           |                                                               | <p>부서졌습니다. 내부 디스크는 신생 내막 조직에 완전히 통합되었습니다. 조직학적 분석은 돼지의 내외부 디스크 주위에서 약간 더 많은 염증 징후를 보였습니다. 두 동물 모두에서 멀티 필라멘트는 디스크 재료에서보다 약간 더 많은 염증성 징후를 나타냈으며, 이는 더 큰 표면적으로 인해 다중 봉합에서는 일반적입니다.</p> <p>조직 형태학적 측정법, 캘리퍼를 이용하여 혈관 직경을 측정하는 조직 형태학적 측정법 및 색조 도플러 초음파를 이용하여 혈관 직경을 측정하는 조직 형태학적 측정법 등 세 가지 다른 방법을 사용하여 5주 후 혈관 개방성을 측정했습니다. 양의 평균 혈관 개방성은 방법에 따라 60%에서 80% 사이였습니다(12회 관측치). 돼지의 평균 혈관 개방성은 40%에서 80% 사이였습니다(2회 관측치).</p> |
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| 최초의 사람 대상 임상 시험                                                                                                                                       |                              |                    |                                                                                                           |                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                       |
| 연구 이름                                                                                                                                                 | 연도/CI                        | 연구 유형              | 연구 목표                                                                                                     | 주요 단계                                                         | 잠재적인 허용 기준                                                                                                                                                                                                                                                                                                                                                                                                            |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology | 2004 Radi Medical Systems AB | 오픈 라벨, 단일군, 다기관 시험 | 본 연구의 목적은 대퇴동맥 접근을 이용한 심장 진단 또는 심장 중재 시술을 받는 환자에서 FemoSeal Vascular Closure System(FemoSeal System)을 사용하여 | 2개 파트 연구<br>총 인원= 80명<br>파트 1 인원= 20명<br>파트 2 인원= 60명<br>적응증: | <p>결과</p> <p>- 압박 없이 FS로 수행된 지혈</p> <p>- 파트 1 20/20(100%)</p> <p>- 파트 2 58/60(97%)</p>                                                                                                                                                                                                                                                                                                                                |

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| Procedures (EU-SE-001); 2004, Radi Medical Systems AB. |  |  | 의 일반적, 그리고 특히<br>불합 부품에<br>대한 안전성, 성능 및<br>유효성을 확인하는<br>것입니다. | 파트 1 - 대퇴 동맥을 접근<br>부위로 사용하는 진단적 심장<br>카테터 삽입<br><br>파트 2 - 대퇴 동맥을 접근<br>부위로 사용하여 진단 및 심장<br>중재 시술을 받는 환자<br><br>30일 추적관찰 | <p>시술 시 지혈까지의<br/>중양값(파트 2) -<br/>1.0분(즉각적인 범위 - 8<br/>분)</p> <p><u>보행까지의 시간(분)</u></p> <p>파트 1 -<br/>중양값: 33.0<br/>평균: 67.8</p> <p>파트 2 -<br/>중양값: 45<br/>평균: 87.5</p> <p><u>주요 혈관 합병증의<br/>발병률 - 30일 추적관찰</u></p> <p>파트 1<br/>-혈관 합병증 없음<br/>20/20(100%)</p> <p>파트 2<br/>가성 동맥류 -<br/>1/59(1.69%)</p> <p><u>치료 실패</u></p> <p>파트 1 - 0/20(0%)</p> <p>파트 2 - 3/60(5%)</p> <ul style="list-style-type: none"> <li>2건은 압박 없이<br/>지혈을 못 함</li> <li>1건은 주요 혈관<br/>합병증, 가상 동맥류</li> </ul> <p><u>지속성 삼출</u></p> <p>파트 1 - 0/20(0%)</p> <p>파트 2 - 8/60(13%)</p> <p><u>혈종</u></p> <p>파트 1 - 0/20(0%)</p> <p>파트 2 - 6/60(10%)</p> |
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FemoSeal™ VCS의 시판 전 개발 계획에 따라 3건의 동물 기능성 실험이 완료되었습니다. 임상 연구 시작 전인 2000년에 동물 연구를 수행하여 FemoSeal™ VCS의 생체 기능성을 평가했습니다. 이 연구에서는 생리적 기능을 유지하는 봉합 부품의 능력 및 분해 수준을 평가했습니다. 18개월 시점에 관내 섬유 조직으로 대체되어 내부 및 외부 디스크 물질은 더 이상 보이지 않았습니다. 결론적으로, 순환계에서 사용했을 때 생리적 기능을 유지하는 FemoSeal™ VCS closure 부품의 기능이 확인되었습니다.

2002년 혈관계에서 지혈하도록 고안된 생분해성 임플란트인 FemoSeal™ VCS의 생체 적합성 및 생체 기능성을 평가하기 위해 동물 연구를 수행했습니다. 요약하면, 임플란트의 분해는 36주까지 거의 완료되었고 유의미한 조직 이상 반응은 없었습니다.

2002년에 시행한 또 다른 동물 연구에서는 혈관계에서 지혈하도록 고안된 생분해성 임플란트인 FemoSeal™ VCS의 생체 적합성과 생체 기능성을 평가했습니다. 5주 후에 디스크의 피막 형성이 완료되었으며, 내외부 디스크에 분해의 징후가 관찰되었습니다. 결론적으로, 순환계에 사용될 때 생리적 기능을 유지하는 임플란트의 기능이 확인되었습니다.

FemoSeal™ VCS 임상 개발 계획의 일환으로 Radi Medical System AB는 시판 전 임상 연구를 수행했습니다. 본 임상연구는 온라인에 게시되거나 제공되지 않습니다. 장치 모델 #11200을 사용한 연구는 유럽 표준 EN 540(인간 피험자용 의료기기의 임상 조사) 및 임상시험을 위한 ICH 일반 고려사항 및 우수 임상 실무 지침에 따라 2002년에서 2004년 사이에 실시되었습니다. 이 연구의 세부 사항은 보고서 EU-SE-001에 문서화되어 있습니다. 본 임상 시험은 Radi Medical Systems AB의 "진단/중재 심장 시술 후 대퇴 동맥 천자 지혈을 위한 FemoSeal 혈관 봉합기구의 다기관 임상 시험"의 최종 보고서에 문서화되었습니다. 본 임상 연구는 FemoSeal™의 첫 번째 모델 #11200으로 수행되었으며 이식형 봉합 구성품의 안전성과 유효성에 중점을 두었습니다. 첫 번째 모델 #11200과 현재 모델 C11202 사이에 유일하게 다른 점은, 프랑스 크기 각각 6F 및 7F와 개선된 전달 체계입니다. 임상적 이점, 용도, 작동 원리, 이식형 봉합 부품의 원자재, 내부셀 및 외부 잠금 디스크는 변경되지 않았습니다.

장치의 용도는 대퇴 동맥을 접근 부위로 사용하여 진단 및 심장 중재 시술을 받는 환자를 위한 것입니다. 이 연구의 목적은 FemoSeal™ VCS의 안전성, 성능 및 유효성을 확인하는 것입니다. 이는 30일 추적관찰을 통한 전향적, 다기관, 단일군 오픈 라벨 연구입니다.

주요 평가변수는 활발한 출혈의 부재로 정의된 지혈까지의 시간입니다. 일차 안전성 변수는 30일 동안 주요 혈관 합병증이 발생한 것입니다. 이차 변수에는 보행 시간, 치료 실패 비율, 이상 반응 발생률, 전달 및 배치 중 기기 성능 특성이 포함되었습니다.

본 연구에 참여한 환자는 동의를 구할 수 있으며, 최소 1회의 온전한 페달 맥박이 있는 성인입니다. 다음 조건 중 하나라도 있는 환자는 연구에서 제외되었습니다.

- 말초혈관질환 병력이 있는 경우
- 자기 면역 질환이 있는 경우
- 중증 빈혈로 알려진 출혈 장애가 있는 경우
- INR >1.5의 경우
- 72시간 이내에 심근경색이 있었던 경우
- 치료에도 불구하고 조절되지 않는 고혈압이 있는 경우
- 셀딩거(Seldinger) 기술로 비만을 막은 경우
- 동맥 절개 부위에 혈관 이식물 또는 스텐트가 있는 경우
- 3개월 이내에 동측 천자가 발생한 경우
- 기대 수명이 6개월 이내인 경우

또한 다음 중 하나가 발견될 경우 환자를 수술 중 검사하고 연구에서 제외했습니다:

- 총 대퇴 동맥의 내강 직경 <5mm
- 천자 부위에 근접한 2cm 이내의 동맥 분지
- 천자 부위에 있는 3cm 이내의 유의미한 협착
- 사용한 1차 유도관이 >6Fr
- 대퇴 동맥 분기점 또는 분기점의 말단에 천자 존재
- 여러 개의 대퇴 동맥 천자 존재
- 후방 대퇴 벽 천자로 알려지거나 의심되는 경우
- 시술 완료 시 큰 혈종(2:6cm)이 있는 경우
- 조직 또는 혈관이 꼬여 시술을 위한 1차 도관 삽입이 어려운 경우

이 단일 프로토콜 연구는 두 부분으로 수행되었습니다. 20명의 환자를 파트 1에 등록한 후, 안전 분석을 완료하고, 이어서 추가 60명의 환자를 파트 2에 등록하였습니다.

파트 1에서 등록한 환자의 평균 나이는 65.9세이고 70.0%가 남성이었으며 95%는 병용 약물을 복용하고 있었습니다. 파트 2의 환자 평균 연령은 63.8세이고 78%는 남성이었으며 100%가 병용 약물을 복용하고 있었습니다.

진단(파트 1 및 파트 2) 또는 중재(파트 2) 심장 카테터 삽입 시술을 받는 환자는 이 연구에 등록할 자격이 있습니다. 이 시술은 각 등록 병원에서 표준 치료에 순응한 후 FemoSeal™ VCS를 사용했습니다. 환자 데이터는 시술 중 및 시술 후 1일 및 30일에 기준으로 수집되었습니다. 결과가 표 1.5에 요약되어 있으며 FemoSeal™ VCS가 이 환자 모집단에서 사용하기에 안전하고 효과적임을 나타냅니다.

표 1.5 시판 전 연구에서 보고된 임상 결과

|                                      | 파트 1   | 파트 2               |
|--------------------------------------|--------|--------------------|
| 환자 수                                 | 20     | 60                 |
| 평균 지혈 시간                             | 1.2분   | 1.6분 <sup>a</sup>  |
| 보행까지 평균 시간                           | 72.2분  | 87.5분 <sup>b</sup> |
| 주요 혈관 합병증의 발병률 <sup>c</sup>          | 0(0%)  | 1(2%)              |
| 이상반응이 있는 환자 수                        | 5(25%) | 19(32%)            |
| 치료 실패(주요 혈관 합병증, 수동 압박의 필요성, 또는 둘 다) | 0(0%)  | 3(5%)              |
| 기기의 오작동                              | 0(0%)  | 6(10%)             |

<sup>a</sup>2명의 환자가 이전의 동측 천자로 인해 시술 시점에 지혈이 안 됐기 때문에 총 표본 크기 58을 기준으로 함. 이 환자들은 7분 및 37분에 지혈이 이루어졌음.

<sup>b</sup>총 표본 크기 59명 기준: 환자 1명은 폐부종으로 인해 인공호흡기를 착용했고 1주일 이상 보행할 수 없어서 포함되지 않았습니다.

<sup>c</sup>수혈 또는 외과적 수복이 필요한 혈관 합병증 또는 항생제 투여, 입원이나 입원 연장, 또는 부위 피사조직 제거가 필요한 국소 감염으로 정의됨

본 연구의 파트 1에서는 주요 혈관 합병증이 관찰되지 않았습니다. 본 연구의 파트 2에서는 시술 후 1일 이내에 보고된 가성 동맥류와 같은 1건의 주요 혈관 합병증이 보고되었습니다. 그 결과 초음파 유도 압박과 가성 동맥류에 트롬빈 주입이 필요했고 환자의 입원이 연장되었습니다.

본 연구 파트 1에서 보고된 5건의 이상 반응 중, 기기와 관련될 수 있는 이상 반응 1건이 있었습니다. 이는 시술 후 1일 차에 심각하지 않은 급격한 출혈 증상이었습니다. 본 연구의 파트 2에서 보고된 19건의 이상반응 중 3건의 장치 관련 혈종의 심각하지 않은 이상 반응이 있었으며, 6건의 장치 관련 비중증 이상 반응이 관찰되었는데 여기에는 지속적 삼출 3건, 혈종 2건 및 운동 후 다리 통증 1건이 있습니다.

파트 2에서는 3명의 환자가 치료 실패로 간주되었습니다. 2명은 압박을 사용하지 않아 지혈을 달성하지 못했으며, 1명은 주요 혈관 합병증(가성 동맥류)으로 인한 것이었습니다. 본 연구의 파트 1에서는 치료 실패가 없었습니다.

본 연구의 파트 2에서 6건의 장치 오작동 중 3건은 시술에 방해되지 않았고, 사용자 오류 1건, 유도관 누출 1건 및 필라멘트 접합부 파손 1건이었습니다. 마지막 두 건은 C11202에서 구현된 모델 업데이트로 해결되었습니다.

시판 전 임상 연구에서 파트 2는 환자의 치료 지시 불이행으로 인해 6개월 추적관찰 결과를 보고하지 않았습니니다. 임상 문헌의 추적관찰 기간과 일치하는 시판 전 임상 연구(EU-SE-001) 30일 결과는 FemoSeal™ VCS가 안전하고 효과적임을 입증합니다.

#### 1.4.2 시판 후 임상 연구의 데이터 요약

완료된 시판 후 임상 연구 4건이 아래 표 1.6에 설명되어 있습니다. 이러한 임상 시험은 온라인에서 공개되거나 제공되지 않습니다.

표 1.6 시판 후 임상 연구

| 시판 후 임상 연구 완료                                                                               |                                                           |                          |                                                                                                                                                                                                                                              |                                                                                                                                                                |                                                                         |
|---------------------------------------------------------------------------------------------|-----------------------------------------------------------|--------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|
| 연구 이름                                                                                       | 연도/CI                                                     | 연구 유형                    | 연구 목표                                                                                                                                                                                                                                        | 주요 단계                                                                                                                                                          | 잠재적인 허용 기준                                                              |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI                                              | 시판 후 연구, 새로운 포장의 사용자 수용성 | FemoSeal Vascular® Closure System #11202 모델 업데이트에 대해 시판 후 연구가 수행되었으며, 이는 첫 번째 모델 #11200과 비교하여 수정된 전달 시스템을 통한 기능성을 문서화합니다.<br><br>이 연구의 목적은 의사와 간호사를 위한 교육 프로젝트인 개정된 사용 지침(IFU)에 대한 피드백을 얻고 위험 분석에서 수행된 평가를 확인하며 제품의 품질 개선에 대한 의견을 제공하는 것입니다. | 환자 100명<br>• 남성 63명/여성 37명<br>• 여성 평균 연령 68세, 남성 평균 연령 65세<br><br>스웨덴 병원 2곳, 의사 6명<br><br>장치 112대<br><br>환자 기록 양식(CRF)에 캡처된 데이터<br><br>계획된 관찰 시간 - 적용 시점부터 30분 | 결과<br>1. 유익하고 적절한 것으로 간주되는 IFU의 그림/지침<br>2. 즉각적인 지혈(91/100)             |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)           | Dr. Nicolas Moes<br>Innsbruck Medical University, Austria | 시판 후 확인 평가               | 본 연구의 목적은 7F 도관으로 수행된 진단적 심장 카테터 삽입 또는 경피적 심장 중재 시술을 받는 환자의 정상적인 임상 절차에서 사용된                                                                                                                                                                 | 지속적으로 참여하는 환자 50명<br><br>지침 - 총 대퇴 동맥의 진단 또는 침습적 심장 카테터 삽입                                                                                                     | 일차 평가변수<br>• 일차 효능 변수 - 진물이 있을 수도 있지만 추가적인 수동 혹은 기계적 압박은 없는 TTH(지혈 시간). |

|                                                                                |            |         |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                          |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|--------------------------------------------------------------------------------|------------|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|-----|----------|-------|----------|-----------|----|-----------|-----------|-------------------------|----------|--------------------|------------|---------------------|-----------|-------------------|---------|-----------------------|----------|--------------------------------|----------|----------------------|-----------|--------------------------|-----------|-----------------------------------|----------|----------------------|--------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                |            |         | FemoSeal®의 안전성과 성능을 평가하는 것입니다.                                                                                                                                                                                            | <table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                                                                                                                                                                                                                                        | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | <ul style="list-style-type: none"><li>• 안전성 변수 - 이상반응 발생률 - 경미하고 중대한 혈관 합병증 및 기타 모든 부작용 – 연구 기간 동안 중증 및 비중증(예: 환자가 퇴원할 때까지).</li></ul> <p>결과</p> <ul style="list-style-type: none"><li>• 평균 지혈 시간</li><li>• 진단 - 56.6 ± 29초</li><li>• 중재 59.9 ± 16.2초</li><li>• 모든 환자 57.8 ±26.3</li><li>• 모든 환자는 4시간 동안 침대에서 휴식을 취한 후 아무 문제 없이 보행할 수 있었습니다.</li></ul> <p>안전성 결과</p> <ul style="list-style-type: none"><li>• 49/50(98%)는 퇴원할 때까지 혈관 합병증이 없었습니다</li><li>• 평균 퇴원 시간 2.6일</li><li>• 1/50(2%)는 혈관 조영술 당일 별다른 일 없이 보행 후 다음날 경미한 출혈 발생</li></ul> |
| n                                                                              | 50         |         |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                          |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| men                                                                            | 35 (70%)   |         |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                          |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| women                                                                          | 15 (30%)   |         |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                          |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| PCI cases                                                                      | 15         |         |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                          |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| age (yrs)                                                                      | 62.8±11.1  |         |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                          |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| body mass index (kg/m²)                                                        | 25.4±6.7   |         |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                          |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| systolic BP (mmHg)                                                             | 131.2±20.9 |         |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                          |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| diastolic BP (mmHg)                                                            | 77.9±10.6  |         |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                          |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| diabetes mellitus                                                              | 9 (18%)    |         |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                          |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| arterial hypertension                                                          | 34 (68%)   |         |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                          |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| previous coronary intervention                                                 | 13 (26%)   |         |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                          |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| preprocedure aspirin                                                           | 50 (100%)  |         |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                          |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| preprocedure clopidogrel                                                       | 50 (100%)  |         |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                          |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Procedural unfractionated heparin                                              | 15 (30%)   |         |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                          |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Procedural abciximab                                                           | 2 (4%)     |         |                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                          |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009) | 2009 RADI  | 시판 후 연구 | <p>본 연구에서는 고객/사용자가 새 패키지, 특히 Tuvek/PET-PE 파우치의 멸균되지 않은 외부 측면 문제를 인지했는지 알려줍니다.</p> <p>본 연구는 이를 다루는 의사가 이전에 사용한 기기와 비교하여 본 기기의 적용/배치 단계에서 차이를 인지하는지에 대한 정보도 제공합니다.</p> <p>또한 본 연구는 제품 품질 개선에 대한 추가 요구 사항에 대한 의견을 제공합니다.</p> | <p>장치 25대<br/>스웨덴 병원 4곳</p> <p>환자의 16/25(64%)은 항응고 약물을 과하게 복용하는 PCI 환자</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | <p>결과</p> <ol style="list-style-type: none"><li>1. 포장 관련 문제 - 21/25(84%)은 적용이 성공적이었으며, 4/25(16%)는 적용이 성공적이지 않았습니니다(1 - 새로운 유도관 테스트, 지지 단계에서 1개의 내부 디스크는 동맥 절개를 함, 버튼을 위로 당기고 외부 디스크를 절개 조직관에 배치, 배치 문제가 없음에도 2번 즉각적인 지혈이 되지 않음)</li><li>2. 즉각적으로 지혈된 환자 19/25(76%)</li><li>3. 출혈 11/25(44%) - 9/25(36%) 진물/출혈, 2/25(8%) 혈중</li></ol> <p>총 문제 발생률 19%</p> |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |

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|----------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|----------------------------|---------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022)</p> | <p>2022/Terumo Medical Corporation</p> | <p>전향적, 다기관, 관찰적, 시판 후</p> | <p>경피 혈관 내 시술받는 실제 대상에서 총 대퇴 동맥(CFA) 접근 부위의 지혈에 있어 FemoSeal™ VCS의 안전성과 유효성을 추가로 입증하기 위함</p> | <ul style="list-style-type: none"> <li>• 병원 방문 또는 전화 통화를 통한 30일(± 7일)의 환자 추적 관찰.</li> <li>• 등록: 2021년 12월부터 2022년 7월까지.</li> <li>• FemoSeal™이 사용되는 진단 또는 중재적 혈관 내 시술을 받고 있는 시험대상자 230명이 등록했습니다.</li> </ul> <p>3곳의 유럽 현장: 프랑스(환자 92명), 독일(환자 38명), 벨기에(환자 100명).</p> | <ul style="list-style-type: none"> <li>• <b>인구 통계/동반 질환:</b> <ul style="list-style-type: none"> <li>- 성별: 남성 161명(70%)/여성 69명(30%).</li> <li>- 평균 연령: 70 ± 12.</li> <li>- BMI: 26.1 ± 4.95 kg/m2.</li> <li>- 고혈압: 환자 160명(69.6%).</li> <li>- 이상지질혈증: 128명(55.7 %).</li> <li>- 관상 동맥 질환: 42명(18.3%).</li> <li>- 현재 흡연자: 86명(37.6 %).</li> <li>- 이전 흡연자: 66명(28.8%).</li> <li>- 관상동맥 심장 질환: 34명(14%).</li> <li>- 이전 심근 경색 경험: 18명(7.8%).</li> <li>- 말초 동맥 재건술: 12명(5.2%) 경동맥 및 83명(37.5%) 하지 동맥.</li> <li>- 항혈소판 요법(기준치): 21명(91.7%)의 이중 항혈소판 요법(DAPT) 포함 211명(91.7%).</li> <li>- 경구 항응고제: 환자 40명(17.4%).</li> </ul> </li> <li>• <b>중재 특성:</b> <ul style="list-style-type: none"> <li>- 설정: 입원 클리닉 162건(70.4%), 외래 클리닉 68건(29.6%).</li> <li>- 주요 적응증: 절뚝거림 147건(63.9%).</li> <li>- 접근 방법: 전행성 35건(15.3%), 역행성 194건(84.7%).</li> </ul> </li> <li>• <b>일차 평가변수:</b> <ul style="list-style-type: none"> <li>- 통합 안정성(시술 후 6시간 이내에 접근 부위의 주요 합병증이 발생하지 않음) 및 유효성(성공적인 천자 부위 지혈) 평가변수는 전체 분석 세트에서</li> </ul> </li> </ul> |
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|  |  |  |  |  | <p>215/226명(95.1%) [95% CI: 91.46; 97.55] 및 FemoSeal™ 치료 세트에서</p> <p>215/230명(93.5%) [95% CI 89.47, 96.30]으로 달성되었습니다.</p> <p>- 유효성 평가변수는 219/226명(96.9%) CI [93.7, 98.7]의 환자에서 달성되었습니다.</p> <p>- 안정성 평가변수는 220/230명(95.2%)[95% CI: 92.15, 97.90] 환자에서 달성되었습니다.</p> <p>● 이차 평가변수:</p> <p>- 시술 후 6시간 동안 접근 부위의 경미한 합병증 없음은 225/230명(97.8%)[95% CI: 95.00; 99.29]에서 달성되었습니다.</p> <p>- 시술 후 6시간 내지 30일 동안 환자 219/230명(95.2%) [95% CI:91.60; 97.59]에서 접근 부위 주요 및 경미한 합병증이 없었습니다.</p> <p>- FemoSeal™ VCD를 이용한 지혈까지의 중간값 시간: 0.42(0.25; 0.50)분.</p> <p>- 보행까지 중간값 시간: 5.00(4.54; 5.50)분.</p> <p>- 병원 입원 중간값 기간: 23.98(22.72, 25.00)시간.</p> <p>- FemoSeal™ VCS의 사용성: 98.7%의 경우 배치하기 '쉬움' 또는 '매우 쉬움'(21(9.2%)에서 배치하기 '쉬움', 205(89.5%)에서 '매우 쉬움'), 226(98.3%)의</p> |
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|  |  |  |  |  | 경우 배치 시 저항 없음<br>또는 낮음.<br>FemoSeal™ 키트(GW<br>0.038")에 포함된<br>가이드와이어를 사용하여<br>치료한 환자의<br>152/230명(66.1%)이 장치<br>결함이나 부작용 보고 없이<br>FemoSeal™에<br>권장되었습니다. |
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2006년 연구는 전달 시스템이 개선된 현재 기기의 안전성과 유효성을 확인하고 FemoSeal™ VCS IFU 및 교육 프로그램에 대한 피드백을 얻기 위해 수행되었습니다. 이 연구는 100명의 환자를 대상으로 했으며 일차 평가변수는 지혈이 되었는지 여부 또는 추가적인 수동 또는 기계적 압박이 필요한지 여부였습니다. 이 연구는 FemoSeal™ VCS의 적용이 대부분 사례에서 성공적이었다는 결론을 내렸습니다(91%는 즉각적으로 지혈되었습니다).

2008년 연구에서는 환자 50명이 등록되어 7 Fr 도관으로 심장 카테터 삽입을 받은 환자에서 FemoSeal™ VCS가 정상적인 임상 절차 중에 사용되었을 때 FemoSeal™ VCS의 안전성과 성능을 평가했습니다. 본 연구의 일차 평가변수는 추가적인 압박, 즉, 수동 또는 기계적 압박 없이 지혈까지의 시간 및 보행까지의 시간에 대한 데이터를 수집하는 것입니다. 연구 결과에 따르면 평균 지혈 시간은 57.8초였고 모든 환자는 4시간의 침대 휴식 후에 보행을 했습니다.

2009년 연구는 새로운 FemoSeal™ VCS 포장을 평가하는 것이었습니다. 25명의 환자가 이 연구에 등록되었습니다. 일차 평가변수는 사용자가 포장으로 문제를 겪었는지였습니다. 사용자는 새로운 FemoSeal™ VCS 포장과 관련하여 아무런 문제가 없다고 했습니다. 이 연구는 또한 지혈 시간 동안 데이터를 수집했습니다.

2022년 연구는 경피 혈관 내 시술받는 실제 대상에서 총 대퇴 동맥(CFA) 접근 부위의 지혈에 있어 FemoSeal VCS의 안전성과 유효성 데이터를 수집하기 위함입니다. 230명의 환자가 이 연구에 등록되었습니다. 등록의 일차 평가변수는 시술 성공(예: 성공적인 천자 부위 지혈)과 주요 합병증(예: 혈관 손상, 접근 부위 관련 출혈, 접근 부위 감염, 반복적인 수동 압박 및 새로운 접근 부위 관련 동측 급성 다리 허혈)의 감소입니다. 이 연구는 FemoSeal™ VCS가 실제 환경에서 잘 작동하며 말초 혈관 내 시술을 받는 환자에게 효과적인 지혈과 낮은 비율의 접근 부위 합병증을 나타낸다는 결론을 내렸습니다. 이



연구는 지혈까지의 짧은 시간과 우수한 작업자 사용성 피드백을 통해 우수한 성능을 입증했으며, FemoSeal™ VCS는 대퇴골 접근 봉합에 있어 귀중한 장치로 평가되었습니다.

### 1.4.3 시판 후 임상 추적관찰의 데이터 요약

#### 1.4.3.1 완료된 시판 후 임상 추적관찰

완료된 시판 후 임상 추적관찰 활동의 요약은 하기 표 1.7에 기재되어 있습니다.

표 1.7. 시판 후 임상 추적관찰 활동

| 완료된 시판 후 임상 추적관찰 활동                                                       |          |                     |                                                                                                     |                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                    |
|---------------------------------------------------------------------------|----------|---------------------|-----------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 활동 이름                                                                     | 연도/CI    | 연구 유형               | 연구 목표                                                                                               | 주요 단계                                                                                                                                                                     | 잠재적인 허용 기준                                                                                                                                                                                                                                                                                                                         |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021 TMC | 시판 후 임상 조사 - 고품질 조사 | 유럽 연합 시장에 유통된 FemoSeal™ 혈관 봉합 장치의 사용과 관련된 예상 피드백을 수집하기 위한 시판 후 설문조사.                                | <ul style="list-style-type: none"> <li>120건</li> <li>5년 이상의 경험을 가진 전문 의사 8명</li> <li>유럽 내 여러 국가</li> </ul>                                                                | <b>1~5 척도 기기 평가 - 설문조사 문항</b> <ul style="list-style-type: none"> <li>허용 기준 <ul style="list-style-type: none"> <li>3~5 평가는 긍정적인 것으로 간주됨</li> <li>모든 문항은 80% 이상의 긍정적 피드백이 있어야 함</li> </ul> </li> <li>결과 <ul style="list-style-type: none"> <li>설문조사 문항에서 20% 이상의 부정적 응답을 받지 않음</li> <li>제품에 대한 불만 사항이 제기되지 않음</li> </ul> </li> </ul> |
| 20210298 – 0.035" and 0038" Guidewire Clinical Survey Report (2021)       | 2021 TMC | 시판 후 임상 조사 - 고품질 조사 | 유럽 연합 시장에 유통된 6Fr Angio-Seal™ VIP Vascular Closure 장치(VCD)에 포함된 0.035" 가이드와이어 및 8Fr Angio-Seal™ VIP | <ul style="list-style-type: none"> <li>0.035" 와이어 설문조사 <ul style="list-style-type: none"> <li>106건의 설문조사</li> <li>64명의 의사</li> </ul> </li> <li>0.038" 와이어 설문조사</li> </ul> | <b>1~5 척도 기기 평가 - 설문조사 문항</b> <ul style="list-style-type: none"> <li>허용 기준 <ul style="list-style-type: none"> <li>3~5 평가는 긍정적인 것으로 간주됨</li> <li>모든 문항은 80% 이상의 긍정적 피드백이 있어야 함</li> </ul> </li> </ul>                                                                                                                               |

| 완료된 시판 후 임상 추적관찰 활동                                                                                                             |                  |                     |                                                                                                 |                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|---------------------------------------------------------------------------------------------------------------------------------|------------------|---------------------|-------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                 |                  |                     | VCD와 FemoSeal Vascular Closure System에 모두 포함된 0.038" 가이드와이어의 사용과 관련된 예상 피드백을 수집하기 위한 시판 후 설문조사. | <ul style="list-style-type: none"> <li>○ 109건의 설문조사</li> <li>○ 55명의 의사</li> <li>● 12건의 회고 설문조사</li> </ul>                                                                                                                                                     | <ul style="list-style-type: none"> <li>● 결과 <ul style="list-style-type: none"> <li>○ 모든 가이드와이어가 허용 등급을 받음</li> <li>○ 제품에 대한 불만 사항이 제기되지 않음</li> </ul> </li> </ul>                                                                                                                                                                                                                                                                                                                                                                                             |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024 TMC/TE | 시판 후 임상 조사 - 고품질 조사 | EU 시장에서 유통되는 가이드와이어를 포함한 FemoSeal VCS 사용과 관련된 예상 피드백을 수집합니다.                                    | <ul style="list-style-type: none"> <li>● 126건의 설문조사</li> <li>● 7개의 현장</li> <li>● 5개의 국가</li> <li>● 2023년 11월 14일-2024년 6월 11일</li> <li>● 의사의 의학 전문 분야: <ul style="list-style-type: none"> <li>○ 혈관 외과</li> <li>○ 중재 방사선</li> <li>○ 혈관학</li> </ul> </li> </ul> | <b>5 척도 기기 평가 - 설문조사 문항</b> <ul style="list-style-type: none"> <li>● 허용 기준 <ul style="list-style-type: none"> <li>○ 3~5 평가는 긍정적인 것으로 간주됨</li> <li>○ 모든 문항은 80% 이상의 긍정적 피드백이 있어야 함</li> <li>○ 이 설문조사에서 이상 반응이 발생하는 경우, 위험 관리에서 예상 가능한 부작용이어야 합니다.</li> </ul> </li> <li>● 환자 인구학적 정보 <ul style="list-style-type: none"> <li>○ 여성: 29.4% (37/126)</li> <li>○ 남성: 69.8% (88/126)</li> <li>○ 성별 공개하지 않음: 0.8 (1/126)</li> <li>○ 연령 &gt;75세: 31.7%</li> </ul> </li> <li>● 결과 <ul style="list-style-type: none"> <li>○ FemoSeal™ VCS와 함께 제공되는</li> </ul> </li> </ul> |

| 완료된 시판 후 임상 추적관찰 활동 |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|---------------------|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                     |  |  |  |  | <p>가이드와이어:<br/>101/126 (80.2%).</p> <ul style="list-style-type: none"> <li>○ 절차 지속<br/>시간(분):<br/>63.4(36.6)(평균<br/>(SD)); 57.0(36.0-<br/>81.0)(중간 (IQR))</li> <li>○ 모든 FemoSeal™<br/>VCS 성능 평가는<br/>긍정적이었습니<br/>다.</li> <li>○ 모든 FemoSeal™<br/>VCS 공급<br/>가이드와이어의<br/>평가는<br/>긍정적이었습니<br/>다.</li> <li>○ 1 건의(0.8%)<br/>이상 반응:<br/>지혈을 위해<br/>수동으로<br/>압박해야 하는<br/>딱딱한 가이드<br/>와이어(Boston<br/>Scientific Amplatz<br/>Super Stiff, 75cm,<br/>0.035인치)를<br/>사용했기 때문에<br/>FemoSeal™ VCS<br/>디스크가 잘<br/>정렬되지 않았을<br/>가능성이 큼니다.</li> </ul> |

Terumo Medical Corporation은 현재 보고 기간(2019년 9월 1일 - 2024년 8월 31일)에 3건의 의사 사용자 고품질 설문조사를 완료했습니다.

FemoSeal™ Clinical Surveys는 임상 사용 중 FemoSeal™ VCS의 안전성 및 성능과 관련하여 사전 예방적 임상 데이터를 수집했습니다. 이 설문 조사에는 전체 장치와 0.038" 가이드와이어를 비롯한 관련 액세서리 및 이들의 직접적인 상호작용에 초점을 맞춘 질문이 포함되었습니다. 가이드와이어 임상 설문조사에서는 FemoSeal™ VCS와 함께

제공되는 0.038" 가이드와이어를 임상적으로 사용하는 동안 안전성 및 성능과 관련하여 사전 예방적 임상 데이터를 수집했습니다. 본 설문 조사 질문은 특히 가이드와이어의 일반적인 사용에 초점을 맞추었으며, 가이드 와이어는 시술용 도관을 통해 혈관 구조에 삽입되는 것부터 와이어 제거에 이르기까지 다양합니다.

기기에 포함된 FemoSeal™ VCS 및 0.038" 가이드와이어는 모든 허용 등급을 받았으며 고품질 임상 조사에서 받은 의견 평가에 기초하여 장치에 대해 6건의 불만이 제기되었으며 가이드와이어에 대해 9건의 불만이 제기되었습니다. 불만 사항은 FemoSeal 및 가이드와이어 모두에 대해 평가되었으며 테루모 시판 후 감시 프로세스의 일부로 평가되었습니다. 확인된 새로운 위험 및/또는 위험 수준이 없었습니다.

PMCF 활동의 일환으로 2024년에 의사 사용자 설문조사가 완료되었습니다. 설문조사 결과 FemoSeal™ VCS 성능 등급 및 안전성이 전반적으로 매우 긍정적인 것으로 나타났습니다. FemoSeal™ VCS와 함께 제공된 하나의 표준 이외의 다른 가이드와이어의 호환성도 입증되었습니다.

#### 1.4.3.2 진행 중/계획된 시판 후 임상 추적관찰

TMC에는 2개의 진행 중/계획된 시판 후 임상 추적관찰 활동이 있습니다. EU 시장에서 FemoSeal VCS가 배포한 가이드와이어 사용 관련 피드백을 전향적으로 수집하기 위해 임상 설문 조사가 완료될 것입니다. 의사가 시술 중에 어떤 가이드와이어를 사용했는지 조사하고자 본 설문 조사를 실시합니다. 이 설문조사의 목적은 FemoSeal™ VCS와 Terumo가 아닌 다른 브랜드의 가이드와이어의 호환성에 대한 문헌 및 외부 검토자의 의견 부족으로 확인된 격차를 해결하는 것입니다. 피드백에는 다양한 가이드와이어가 있는 장치의 성능과 관련된 기술적 결과, 임상 성능 및 안전성이 포함됩니다.

#### 1.4.4 체계적인 문헌 검토의 데이터 요약

Terumo Medical Corporation은 Angio-Seal™ VIP Vascular Closure 기기 및/또는 이와 유사한 기기에 대해 공개된 시험에서 얻은 임상 안전성 및 성능 데이터를 수집하고 평가하기 위해 체계적인 문헌 검토를 수행합니다. 매년 간행되는 문헌을 심사하는 목적은 알려지지 않은 부작용을 식별하고, 알려진 부작용을 모니터링하며, 응급 위험을 식별하고 FemoSeal™ VCS의 체계적인 오용 또는 오프 라벨 사용을 식별하는 것입니다.

2019년 9월 1일부터 2024년 8월 31일까지 기간을 포함하는 가장 최근의 체계적 문헌 검토는 FemoSeal™ VCS에 대한 임상 안전성 및 성능 데이터를 제공하는 12건의 공개된 시험을 확인하였습니다. 23건의 참고문헌에서 FemoSeal™ VCS의 온 라벨 사용이 보고되었으며 9건의 연구에서 오프 라벨 사용이 보고되었습니다. 전체적으로 FemoSeal™ VCS 사용에 대해 특정된 연구의 문헌 검토는 경피 혈관 카테터 삽입 시술을 받는 EU 내

환자를 대표하는 연구의 모집단을 보여줍니다. 이 23개의 온 라벨 상호 검토 간행물 목록은 **섹션 3**을 참조하십시오.

임상 성능은 다음의 측정으로 평가했습니다.

- 지혈까지의 시간은 일반 경피적 대퇴동맥 봉합을 위한 최신 기술보다 낮거나 이와 비슷합니다.
- 보행까지의 시간은 일반 대퇴동맥의 경피적 봉합을 위한 최신 기술보다 낮거나 이와 비슷합니다.
- 수술 후 합병증 비율은 현재의 표준 치료보다 비슷하거나 낮습니다.

이러한 임상 성능 측정을 토대로, 본 문헌 검토의 데이터는 FemoSeal™ VCS가 7Fr 이하의 시술용 도관을 사용하여 경피 카테터 삽입을 받은 환자에서 대퇴 동맥 천자(동맥 절개술)를 지혈하는 데 성공적으로 사용될 수 있음을 보여주었습니다. 대부분의 환자(79.65~100%)에서 완전한 지혈이 이루어졌으며 지혈까지의 중간 시간은 0.5분, 퇴원까지의 평균 시간은 3일이었습니다. 69.2~86.7%의 환자가 수술 종료 후 5시간이 지난 후 보행할 수 있었으며, 수술 후 평균 침상 안정 시간은 349분이었습니다. FemoSeal™ VCS 실패는 3.68~4%의 경우에서 관찰되었으며, 0.9~4.4%의 시술에서 추가적인 수동 압박이 필요했습니다.

임상 안전성은 다음과 같은 이상 반응에 의해 평가되었습니다:

- 출혈
- 혈종
- 가성 동맥류
- 타박상
- 동정맥루
- 감염 증상
- 사망

이러한 이상반응과 관련하여 포함된 연구에서 FemoSeal™ VCS에 대해 보고된 발생률은 수동 압박 및 기타 혈관 지혈 장치와 관련하여 지금까지 보고된 비율보다 낮거나 비슷했습니다.

새로운 위험, 예상하지 못한 위험, 새롭게 부상한 위험 또는 용인할 수 없는 위험이 확인되지 않았기 때문에 10건의 사례 보고서 검토에서 이상반응이 확인되지 않았습니다.

진단 혈관조영술 또는 중재 수술 중 FemoSeal™ VCS 사용의 전반적인 효과는 성별, 연령, 환자 해부학적 구조, 동반 질환, 천자 부위의 해부학적 배치, 외과의사의 경험, VCD 배치 방법, 수술 후 관리 등과 같은 여러 요인에 따라 달라집니다. 지혈 달성을 포함한 기술적 성공 외에도 FemoSeal™ VCS는 지혈까지의 시간 단축, 보행까지의 시간 단축과 같은 대퇴 동맥 천자 후 혈관 봉합과 관련된 임상적 이점을 제공했습니다. FemoSeal™ VCS에 대한 성능 결과는 의도된 대로 사용될 때 이러한 유형의 장치에 대해 예상되는 성능 결과와 일치합니다. 현재 검색 기간 동안 검색된 참고 자료 중 일부는 공통 대퇴 동맥 이외의 해부학적 위치에서 대상 기기를 사용하고 오프 라벨로 간주되는 동맥절개술 > 7 Fr의 봉합을 위해 사용한 것으로 나타났습니다.

검토 중에 알려지지 않은 부작용, 발생 위험 또는 장치의 체계적인 오용 가능성은 확인되지 않았습니다. 그러나 FemoSeal™ VCS를 숙련된 의사가 조심스럽게 사용하는 경우 의료 장치는 유용한 필수 임상 장치로 효과를 발휘합니다. 전반적으로, 표적 요법 및 FemoSeal™ VCS는 현재 혈관 접근 관련 합병증 치료에 존재하는 임상적 필요를 해결합니다.

전반적으로, 본 문헌 검토의 데이터는 이전에 알려지지 않은 임상 환경에서의 성능 또는 안전성 문제, 또는 예상/허용 가능 비율보다 높은 비율로 발생한 이상 반응을 식별하지 않았습니다. 따라서, 이 문헌 검토를 통해 경피 카테터 삽입 후 동맥 절제술에서 지혈을 위한 압박 시 FemoSeal™ VCS를 사용할 경우 예상대로 계속 작동하며 심각한 안전 문제와 관련이 없다는 결론을 내릴 수 있습니다.

#### 1.4.5 시판 후 조사 데이터 요약

사전적 PMS 시스템을 마련하고 모든 불만 사항을 월 단위로 내부 제조 절차를 준수하여 검토합니다. 불만 데이터는 2019년 9월 1일부터 2024년 8월 31일까지의 기간 동안 분석되었습니다, 전체적으로 28건의 의료기기 감시(MDV) 보고서와 476건의 고객 불만 보고서가 제조업체에 제출되었습니다. 28건의 MDV 보고 중 27건은 이상 반응과 관련이 있었고 1건은 장치 오작동과 관련이 있었습니다. 보고 기간 동안 2건의 사망이 있었지만, 보고된 사망 중 대상 장치와 관련된 것으로 판단된 사망은 없었습니다. 제조업체에 제기된 476건의 불만사항 중 가장 일반적인 불만사항의 원인은 배치 어려움(146건 발생, 0.0142% 발생률)이었습니다. 빼기 모드의 고장 발생은 0.0126%(130건 발생)의 비율로 두 번째로 많이 발생했습니다.

FemoSeal 혈관 봉합기구는 전 세계적으로 1,030,136개 이상이 판매되었으며 유럽 경제 지역에서는 827,843개가 판매되었습니다. 글로벌 판매량 기준으로 산정된 불만 빈도는 0.046%입니다. 전반적인 고객 불만 비율은 매우 낮습니다. IFU 및 위험 문서에 포함되지 않은 새로운 위험이 확인되지 않았습니다.



바람직하지 않은 부작용에 대한 발생률은 표 1.2에 나와 있습니다. 불만사항 중 예기치 못하거나 새로 생겨나거나 허용되지 않는 새로운 위험은 확인되지 않았습니다. 알려진 바람직하지 않은 부작용의 빈도 또는 중증도에는 유의미한 증가가 없었습니다.

#### 1.4.6 임상 성능 및 안전성에 대한 전반적인 요약

FemoSeal™ VCS는 7F(2.33mm) 또는 더 작은 시술용 도관을 사용하여 경피적 카테터 삽입을 받은 환자의 총 대퇴 동맥 천자(동맥 절개술)를 지혈하는 데 사용됩니다. 이 임상 평가는 FemoSeal™ VCS의 용도와 관련된 시판 전 및 시판 후 임상 데이터 및 문헌에 대한 포괄적인 분석을 기반으로 합니다.

2019년 9월 1일부터 2024년 8월 31일까지의 기간에 걸쳐 발행된 문헌에 대한 포괄적인 검토가 수행되었습니다. 증거 문헌에는 FemoSeal™ VCS에 대한 29건의 연구가 포함되었습니다. 임상 평가에서 제공된 증거는 지시된 대로 사용될 때 대상 기기가 안전하고 효과적이며 정상적인 사용 조건 하에서 기기와 관련될 수 있는 모든 위험 또는 바람직하지 않은 부작용은 환자에 대한 이익과 비교할 때 허용 가능한 위험을 구성한다고 결론지었습니다. 대상 기기에 대한 성능 결과는 의도된 대로 사용될 때 이러한 유형의 장치에 대해 예상되는 성능 결과와 일치합니다.

FemoSeal™ VCS 사용과 관련하여 잠재적으로 바람직하지 않은 부작용에는 동맥 절개술 지혈의 대체 수단에서 흔히 보고되는 부작용이 있습니다(예: 출혈 및 혈종). 전반적으로 FemoSeal™ VCS 사용 시 보고된 부작용 발생률은 수동 압박 및 유사한 혈관 지혈 장치에서 보고된 발생률과 비슷합니다. 특히, 출혈 및 혈종의 경우 FemoSeal™ VCS에 대해 보고된 비율은 유사한 혈관 지혈 장치에 대해 보고된 비율보다 적습니다. 발표된 문헌과 시판 후 조사 모두에서 보고된 각각의 이상 반응은 이전에 확인되었습니다(섹션 1.3 참조).

FemoSeal™ VCS에 대한 임상 안전성 및 성능에 관한 기존 데이터에 따르면 사용 지침에 따라 이 혈관 봉합기구를 사용할 경우 환자가 얻을 수 있는 이점이 발생할 수 있는 위험보다 더 많습니다.

상기 이전 섹션에서 설명한 바와 같이, FemoSeal™ VCS에 대해 제공된 데이터는 평가 중인 기기와 관련된 데이터(예: 기기 사용, 안전성 결과, 임상 성능 및 임상 유익성)와 확인된 동급 기기와 최신 기술에 열거된 유사한 기기와 관련된 데이터 간의 일관성을 보여줍니다.

안전성 데이터의 교차 분석은 다음 간의 불일치를 식별하지 못했습니다.

- 최신 기술에서 언급된 데이터
- 평가 중인 기기에 특정한 데이터

- 위험 관리 파일에 언급된 데이터
- 라벨링 및/또는 IFU에 언급된 데이터(즉, 사용자에게 전달되는 잔여 위험성을 다름).

임상 안전성은 발표된 상호 심사 임상 문헌, 임상시험을 의뢰한 회사, 시장 철회 없이 연결된 시판 후 데이터의 검토에서 확인된 낮은 합병증률로 입증되었습니다. 성능에 대한 우려는 확인되지 않았으며, 검토된 문헌에는 제조업체의 사용 목적과 일치하는 FemoSeal™ VCS의 사용이 포함되었습니다.

## 1.5 가능한 진단 또는 치료 대안

수동 압박은 통상적으로 혈관 카테터 삽입 이후 동맥 절개술 부위의 지혈을 위해 사용됩니다. 수동 압박은 장시간 움직이지 못하고(시술 후 최대 8시간) 상당한 불편함이 있으며 입원 기간이 길어지는 환자들과 관련이 있었습니다. 최근의 체계적인 검토에 따르면 수동 압박으로 지혈하는 데 걸리는 중간값 시간은 20.8분이었습니다.<sup>1</sup>

수동 압박의 대안으로는 동맥 절개술 부위에 기계적 압박을 가하는 외부 지혈 기기가 있습니다. 이러한 장치는 지혈 시간 또는 보행 시간을 단축시키지 않지만, 수동 압박을 기계적 압박으로 대체함으로써 필요한 인력을 줄여줍니다. 기계적 압박 사용과 관련된 이상사례 비율은 수동 압박의 이상사례 비율과 비슷합니다.

FemoSeal™ VCS와 같은 혈관 봉합기구는 동맥 절개를 지혈하도록 고안되었습니다. 이 장치들은 지혈 시간을 단축하고 더 빠르게 보행하는 것을 목표로 합니다. 13개의 상용화된 기기를 포함하는 최근의 체계적인 검토에 따르면, 혈관 봉합 기기로 지혈하는 데 걸리는 중간값 시간은 5.4분이었습니다. 개별 혈관 봉합기구의 지혈에 걸리는 중위 시간은 1분(FemoSeal™ VCS)에서 14분 사이였으며, 대다수 장치는 4분에서 10분 사이였습니다.<sup>1</sup>

수동 압박, 외부 지혈 장치 또는 혈관 봉합기구와 함께 동맥 절개 부위 지혈과 관련하여 흔히 보고되는 이상 반응으로는 혈종, 접근 부위의 출혈, 가성 동맥류, 동정맥류 및 감염이 있습니다. 동일한 체계적인 문헌 고찰(34건의 무작위 대조 시험, 14,401명의 환자)에 따르면, 수동 압박과 혈관 봉합 장치의 사용 사이에서 부작용 발생률이 유사한 것으로 나타났으며, 단, 혈관 봉합 장치로 인해 출혈이 약간 증가하는 경향이 있었습니다.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*



## 1.6 권장 사용자 프로필 및 교육

FemoSeal™ 혈관 봉합기구의 대상 사용자는 총 대퇴 동맥을 통한 혈관 내 시술에 대한 동맥 접근 및 지혈 수행 자격을 갖추었으며 테루모 메디컬 주식회사(Terumo Medical Corporation) FemoSeal™ 의사 교육 프로그램에 참여한 의사입니다.

## 1.7 관련 조화 및 공통 표준

| 표준 참조        | 현재 규정 준수 연도/개정 | 설명                                                                                                                                       |
|--------------|----------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070    | 2014/AMD1:2018 | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070 | 2014/A1:2018   | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA 지침       | 2021년 5월 20일   | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052   | 2015           | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213   | 2017           | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503   | 2020           | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182   | 2019           | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |
| EN ISO 13485 | 2016/A11:2021  | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 13485    | 2016           | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |

| 표준 참조          | 현재 규정 준수<br>연도/개정 | 설명                                                                                                                                                                          |
|----------------|-------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14644-1    | 2015              | Cleanrooms and associated controlled environments<br>— Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1 | 2015              | Cleanrooms and associated controlled environments<br>— Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2    | 2015              | Cleanrooms and associated controlled environments<br>— Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2 | 2015              | Cleanrooms and associated controlled environments<br>— Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3    | 2019              | Cleanrooms and associated controlled environments<br>— Part 3: Test methods                                                                                                 |
| EN ISO 14644-3 | 2019              | Cleanrooms and associated controlled environments<br>— Part 3: Test methods                                                                                                 |
| ISO 14698-1    | 2003              | Cleanrooms and associated controlled environments<br>— Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1 | 2003              | Cleanrooms and associated controlled environments<br>— Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2    | 2003/TC1:2004     | Cleanrooms and associated controlled environments<br>— Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| EN ISO 14698-2 | 2003/TC 1:2004    | Cleanrooms and associated controlled environments<br>— Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| USP <788>      | 해당 없음             | PARTICULATE MATTER IN INJECTIONS                                                                                                                                            |

| 표준 참조          | 현재 규정 준수<br>연도/개정 | 설명                                                                                                                   |
|----------------|-------------------|----------------------------------------------------------------------------------------------------------------------|
| EU 약전 2.9.19   | 해당 없음             | Particulate Contamination: Sub-Visible Particles                                                                     |
| IEC 62366-1    | 2015              | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN 62366-1     | 2015              | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN ISO 14971   | 2019/A11:2021     | Medical devices — Application of risk management to Medical devices                                                  |
| ISO 14971      | 2019              | Medical devices — Application of risk management to Medical devices                                                  |
| ASTM F1980     | 2016              | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1 | 2020              | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1    | 2018              | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2 | 2006              | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2    | 2006              | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3 | 2014              | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3    | 2014              | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4 | 2017              | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4    | 2017              | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |

| 표준 참조           | 현재 규정 준수<br>연도/개정 | 설명                                                                                                                                               |
|-----------------|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-5  | 2009              | Biological evaluation of medical devices – Part 5:<br>Tests for in vitro cytotoxicity                                                            |
| ISO 10993-5     | 2009              | Biological evaluation of medical devices – Part 5:<br>Tests for in vitro cytotoxicity                                                            |
| EN ISO 10993-6  | 2016              | Biological evaluation of medical devices - Part 6:<br>Tests for local effects after implantation                                                 |
| ISO 10993-6     | 2016              | Biological evaluation of medical devices - Part 6:<br>Tests for local effects after implantation                                                 |
| EN ISO 10993-10 | 2023              | Biological evaluation of medical devices —Part 10:<br>Tests for irritation and skin sensitization                                                |
| ISO 10993-10    | 2021              | Biological evaluation of medical devices —Part 10:<br>Tests for irritation and skin sensitization                                                |
| EN ISO 10993-11 | 2018              | Biological evaluation of medical devices — Part 11:<br>Tests for systemic toxicity                                                               |
| ISO 10993-11    | 2017              | Biological evaluation of medical devices — Part 11:<br>Tests for systemic toxicity                                                               |
| EN ISO 10993-12 | 2021              | Biological evaluation of medical devices — Part 12:<br>Sample preparation and reference materials                                                |
| ISO 10993-12    | 2021              | Biological evaluation of medical devices — Part 12:<br>Sample preparation and reference materials                                                |
| EN ISO 10993-17 | 2009              | Biological evaluation of medical devices — Part 17:<br>Establishment of allowable limits for leachable<br>substances                             |
| ISO 10993-17    | 2002              | Biological evaluation of medical devices — Part 17:<br>Establishment of allowable limits for leachable<br>substances                             |
| ISO 10993-18    | 2020/A1:2022      | Biological evaluation of medical devices — Part 18:<br>Chemical characterization of medical device materials<br>within a risk management process |

| 표준 참조           | 현재 규정 준수 연도/개정 | 설명                                                                                                                                                                           |
|-----------------|----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-18 | 2020/A1:2022   | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-23 | 2021           | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23    | 2021           | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382      | 2018           | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756       | 2017           | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>        | 해당 없음          | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>       | 해당 없음          | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72  | 2019           | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135    | 2014/A1:2019   | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135       | 2014/A1:2018   | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7  | 2008/A1:2022   | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |

| 표준 참조          | 현재 규정 준수<br>연도/개정 | 설명                                                                                                                                                              |
|----------------|-------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-7    | 2008/A1:2019      | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                               |
| EN 556-1:      | 2024              | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices |
| EN ISO 11737-1 | 2018/A1:2021      | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11737-1    | 2018/A1:2021      | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| EN ISO 11138-1 | 2017              | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-1    | 2017              | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| EN ISO 11138-2 | 2017              | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 11138-2    | 2017              | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| EN ISO 15223-1 | 2016              | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| ISO 15223-1    | 2016              | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| EN 1041        | 2008/A1:2013      | Information supplied by the manufacturer of medical devices                                                                                                     |
| EN ISO 11607-1 | 2020/A1:2023      | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                         |

| 표준 참조                       | 현재 규정 준수<br>연도/개정 | 설명                                                                                                                                                                                  |
|-----------------------------|-------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11607-1                 | 2019/A1:2023      | Packaging for Terminally Sterilized Medical Devices<br>– Part 1: Requirements for Materials, Sterile Barrier<br>Systems and Packaging Systems                                       |
| EN ISO 11607-2              | 2020/A1:2023      | Packaging for Terminally Sterilized Medical Devices<br>– Part 2: Validation requirements for forming, sealing,<br>and assembly processes                                            |
| ISO 11607-2                 | 2019/A1:2023      | Packaging for Terminally Sterilized Medical Devices<br>– Part 2: Validation requirements for forming, sealing,<br>and assembly processes                                            |
| ASTM D4169                  | 2016              | Standard Practice for Performance Testing of<br>Shipping Containers and Systems                                                                                                     |
| ASTM<br>F1886/F1886M-<br>16 | 2016              | Standard Test Method for Determining Integrity of<br>Seals for Flexible Packaging by Visual Inspection                                                                              |
| ASTM F2825                  | 2018              | Standard Practice for Climatic Stressing of Packaging<br>Systems for Single Parcel Delivery                                                                                         |
| ASTM F2096                  | 2011 (R 2019)     | Standard Test Method for Detecting Gross Leaks in<br>Medical Packaging by Internal Pressurization (Bubble<br>Test)                                                                  |
| ASTM<br>F88/F88M-15         | 2015              | Standard Test Method for Seal Strength of Flexible<br>Barrier Materials                                                                                                             |
| MDCG 2021-24                | 2021              | Guidance on classification of medical devices                                                                                                                                       |
| MDCG 2020-3                 | 2020              | Guidance on significant changes regarding the<br>transitional provision under Article 120 of the MDR<br>with regard to devices covered by certificates<br>according to MDD or AIMDD |
| MDCG 2020-8                 | 2020              | Post-market clinical follow-up (PMCF) Evaluation<br>Report Template A guide for manufacturers and<br>notified bodies                                                                |
| MDCG 2020-7                 | 2020              | Post-market clinical follow-up (PMCF) Plan Template<br>A guide for manufacturers and notified bodies                                                                                |

| 표준 참조          | 현재 규정 준수 연도/개정 | 설명                                                                                                                                                                                                                                                            |
|----------------|----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-6    | 2020           | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                                                                                                          |
| MDCG 2019-9 v1 | 2022           | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                                                                                      |
| MDCG 2019-8 v2 | 2020           | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15   | 2020           | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11   | 2021           | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19   | 2021           | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4 | 2021           | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2    | 2019           | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1    | 2019           | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7    | 2018           | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6    | 2018           | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |



| 표준 참조                  | 현재 규정 준수<br>연도/개정 | 설명                                                                                                                                                                                                     |
|------------------------|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2018-4            | 2018              | MDCG 2018-4 Annex: UDI database<br>Definitions/Descriptions and formats of the UDI core<br>elements for systems or procedure packs                                                                     |
| MDCG 2018-3<br>v1      | 2020              | Guidance on UDI for systems and procedure packs                                                                                                                                                        |
| MDCG 2021-25           | 2021              | Regulation (EU) 2017/745 - application of MDR<br>requirements to 'legacy devices' and to devices placed<br>on the market prior to 26 May 2021 in accordance<br>with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2.12-2<br>Rev 2 | 2012              | Guidance document Medical devices - Market<br>surveillance - Post Market Clinical Follow-up studies -<br>MEDDEV 2.12/2 rev.2                                                                           |

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### 3.0 개정 이력

| SSCP 개정 번호           | 발행일자         | 변경 사항 설명                             | 인증 기관에서 검증한 개정 버전                                                                                                                                                                                                                              |
|----------------------|--------------|--------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022         | 2023년 1월 20일 | 초기 발행, MDR CE 인증                     | <p><input checked="" type="checkbox"/> 예</p> <p>유효성 검증 언어: English</p> <p><input type="checkbox"/> 아니요(등급 IIa 또는 일부 IIb 삽입형 장치(MDR, 제52조 (4) 제2항)에만 해당되며, 이는 SSCP가 아직 NB에 의해 검증되지 않은 경우에 한함)</p> <p><input type="checkbox"/> 기타(구체적으로 명시):</p> |
| SSCP-FS-2023 - 개정판 1 | 2024년 3월 15일 | 2019년 1월 1일부터 2023년 12월 31일까지 업데이트됨. | <p><input checked="" type="checkbox"/> 예</p> <p>유효성 검증 언어: English</p> <p><input type="checkbox"/> 아니요(등급 IIa 또는 일부 IIb 삽입형 기기(MDR, 제52조 (4) 제2항)에만 해당되며, 이는 SSCP가 아직 NB에 의해 검증되지 않은 경우에 한함)</p> <p><input type="checkbox"/> 기타(구체적으로 명시):</p> |
| SSCP-FS-2024 개정판 1   |              | 2019년 9월 1일부터 2024년 8월 31일까지 업데이트됨.  | <p><input type="checkbox"/> 예</p> <p>유효성 검증 언어: English</p> <p><input type="checkbox"/> 아니요(등급 IIa 또는 일부 IIb 삽입형 기기(MDR, 제52조 (4) 제2항)에만 해당되며, 이는 SSCP가 아직 NB에 의해 검증되지 않은 경우에 한함)</p> <p><input type="checkbox"/> 기타(구체적으로 명시):</p>            |

|                       |               |                                |                                                                                                                                                                                                                                                                                                       |
|-----------------------|---------------|--------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>개정판 2 | June 20, 2025 | 검증을 위한 NSAI<br>쿼리를 기반으로<br>수정됨 | <div> <div><input checked="" type="checkbox"/> 예</div> <div>유효성 검증 언어: English</div> </div> <div> <div><input type="checkbox"/> 아니요(등급 IIa 또는 일부 IIb 삽입형 기기(MDR, 제52조 (4) 제2항)에만 해당되며, 이는 SSCP가 아직 NB에 의해 검증되지 않은 경우에 한함)</div> </div> <div> <div><input type="checkbox"/> 기타(구체적으로 명시):</div> </div> |
|-----------------------|---------------|--------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

## Kopsavilkums par drošumu un klīnisko veiktspēju

### FemoSeal™ Vascular Closure System

|                                                                     |                                                                                              |
|---------------------------------------------------------------------|----------------------------------------------------------------------------------------------|
| <b>Ražotājs</b>                                                     | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 ASV          |
| <b>Ražotāja SRN</b>                                                 | US-MF-000019594                                                                              |
| <b>Vadības pārstāvis/par regulatīvajām lietām atbildīgā persona</b> | Kimberlija Feitla (Kimberli Feitl)<br>Vice President, Quality                                |
| <b>Basic UDI-DI</b>                                                 | 38970FS79                                                                                    |
| <b>EMDN numurs</b>                                                  | C900199 — Hemostāzes sistēmas — citas                                                        |
| <b>Ierīces klase</b>                                                | III klase                                                                                    |
| <b>Gads, kad ierīce pirmo reizi saņēma CE zīmi</b>                  | 2005                                                                                         |
| <b>Pārstāvis ES</b>                                                 | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Beļģija<br>SRN: BE-AR-000001433 |
| <b>Pilnvarotā iestāde</b>                                           | NSAI<br>CE 0050                                                                              |

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Šis kopsavilkums par drošumu un klīnisko veikspēju (Summary of Safety and Clinical Performance — SSCP) ir paredzēts, lai sniegtu publisku piekļuvi atjauninātam kopsavilkumam par FemoSeal™ Vascular Closure System (VCS) drošuma un klīniskās veikspējas galvenajiem aspektiem.

Lietotājiem / veselības aprūpes speciālistiem paredzētais kopsavilkums par ierīces drošumu un klīnisko veikspēju ir sniegts tālāk **sadaļā 1.0**.

## **1.0 KOPSAVILKUMS LIETOTĀJIEM / VESELĪBAS APRŪPES SPECIĀLISTIEM**

Ar šo SSCP nav paredzēts aizstāt lietošanas instrukcijas kā galveno dokumentu, lai nodrošinātu, ka ierīce tiek lietota droši, kā arī nav paredzēts sniegt diagnostiskus vai terapeitiskus ieteikumus paredzētajiem lietotājiem vai pacientiem. Ar šo SSCP nav paredzēts aizstāt obligāto informāciju implantu kartēs vai jebkādos citos obligātajos dokumentos.

### **1.1 Ierīces paredzētais lietojums**

#### **1.1.1 Paredzētais lietojums**

FemoSeal™ Vascular Closure System ir medicīniska ierīce, kas paredzēta arteriālās punkcijas slēgšanai pēc perkutānās katetrizācijas, izmantojot kopējo augšstilba artēriju.

#### **1.1.2 Lietošanas indikācijas**

FemoSeal™ Vascular Closure System ir indicēta lietošanai parastās augšstilba artērijas punkcijas (arteriotomijas) slēgšanai pacientiem, kuriem veikta perkutāna katetrizācija, izmantojot 7F (2,33 mm) vai mazāku procedūras apvalku.

#### **1.1.3 Kontrindikācijas un/vai ierobežojumi**

FemoSeal™ Vascular Closure System ir kontrindicēta pacientiem ar arteriotomijām, kurās ir lietoti apvalki vai ierīces, kas lielākas par 7F (2,33 mm).

#### **1.1.4 Mērķa pacientu populācija**

Ir noteikts, ka FemoSeal™ Vascular Closure System ir droša un efektīva pacientiem, kuri sasnieguši vismaz 18 gadu vecumu un kuriem veikta perkutāna katetrizācija, izmantojot 7F (2,33 mm) vai mazāku procedūras apvalku.

#### **1.1.5 Īpašas pacientu populācijas**

FemoSeal™ Vascular Closure System drošums un efektivitāte nav noteikta šādām pacientu grupām:

- Pacienti ar iepriekš esošu autoimūnu slimību.
- Pacienti, kuriem tiek veikta terapeitiskā trombolīze.
- Pacienti ar klīniski nozīmīgu perifēro asinsvadu slimību.
- Pacienti ar nekontrolētu hipertensiju (sistoliskais spiediens > 220 mmHg vai diastoliskais spiediens > 110 mmHg).
- Pacientiem ar asiņošanas traucējumiem, tostarp trombocitopēniju (trombocītu skaits < 100 000) vai anēmiju (Hgb < 10 mg/dl).

- Pacienti, kuru kopējās augšstilba artērijas iekšējais lūmens ir mazāks par 5 mm.
- Pacienti ar nieru un/vai aknu darbības traucējumiem.
- Pacienti ar citu nozīmīgu blakuslimību.
- Iedzīvotāji ar specifisku rases un/vai etnisko piederību.
- Pacienti ar miokarda infarktu pēdējo 72 stundu laikā.
- Pacienti ar asinsvadu transplantātu vai stentu punkcijas vietā.
- Grūtnieces vai patientes, kuras baro bērnu ar krūti.
- pacientiem, kas jaunāki par 18 gadiem.

### 1.1.6 Paredzētie lietotāji

FemoSeal™ Vascular Closure System paredzētie lietotāji ir ārsti, kuri ir apmācīti, lai viņi varētu veikt arteriālo piekļuvi un slēgšanu endovaskulārajās procedūrās, izmantojot kopējo augšstilba artēriju, un ir piedalījušies Terumo Medical Corporation FemoSeal™ ārstu instruēšanas programmā.

## 1.2 Ierīces apraksts

### 1.2.1 Šīs ierīces apraksts

FemoSeal™ Vascular Closure System, ko ražo uzņēmums Terumo Medical Corporation (TMC), ir absorbējama asinsvadu slēgšanas ierīce, kas izstrādāta, lai panāktu augšstilba artērijas hemostāzi pēc perkutānās katetrizācijas, izmantojot kopējo augšstilba artēriju.

FemoSeal™ slēgšanas elementi sastāv no diviem absorbējamiem polimēru diskiem, iekšējā blīvējuma un ārējās bloķēšanas diska, kas tiek turēti kopā ar absorbējamu daudzšķiedru materiālu, tādējādi mehāniski noslēdzot arteriotomiju (sk. **attēlu 1.1** un **attēlu 1.2**). Pēc izvēršanas caur konusa korpusa apvalku ārējais bloķēšanas disks tiek uzspiests uz daudzšķiedru serdeņa, kā rezultātā punkcijas vieta tiek mehāniski noslēgta starp iekšējo un ārējo bloķēšanas disku. Iekšējais blīvējums un ārējais bloķēšanas disks tiek turēti vietā ar berzi uz daudzšķiedru serdeņa. Hemostāzi panāk ar mehāniskiem līdzekļiem. Noslēgšanas elementi tiek noārdīti hidrolīzes rezultātā.

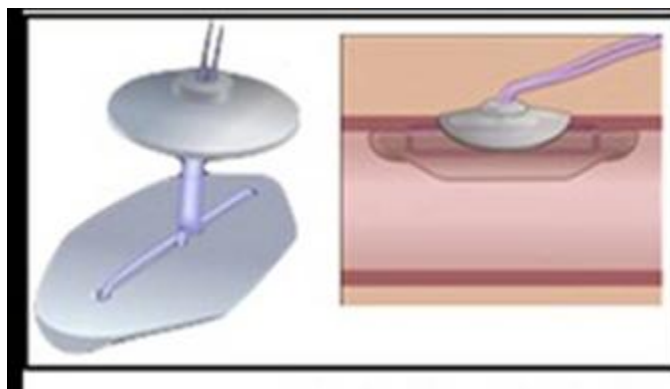
Implantējamie slēgšanas komponenti, iekšējais blīvējums un ārējais bloķēšanas disks noārdās astoņpadsmit (18) mēnešu laikā, savukārt daudzšķiedru materiāls noārdās un tiek absorbēts hidrolīzes rezultātā apkārtējos audos pēc diviem (2) līdz trim (3) gadiem. Implantējamo slēgšanas komponentu spēja saglabāt kompresiju arteriotomijā ir testēta līdz astoņām (8) stundām. Noārdšanās produkti metabolizējas un izdalās ar urīnu vai tiek izelpoti kā oglekļa dioksīds caur

plaušām. Pētījumos ar dzīvniekiem nav novērota uzkrāšanās ietekme. FemoSeal™ papildu komponenti, kas procedūras laikā nonāks saskarē ar dzīvajiem audiem vai asinīm, ir konusa korpusa apvalks, dilatators, bļietēšanas caurulīte, stūmējs un vadītājstīga.

**Attēls 1.1. Attiecīgi iekšējais blīvējums un ārējais bloķēšanas disks**

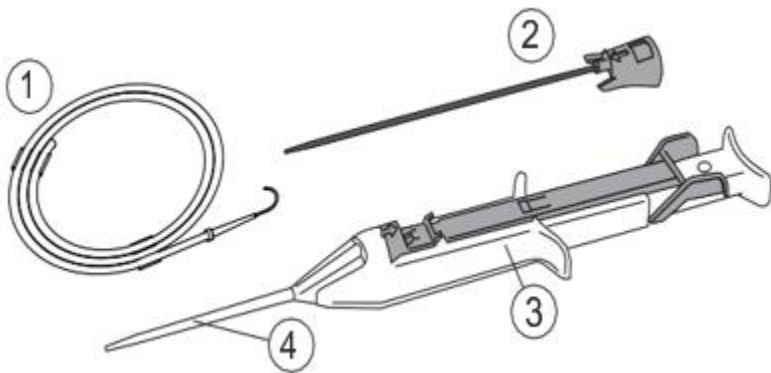


**Attēls 1.2. Iekšējā blīvējuma un ārējā bloķēšanas diska izvietošana**



FemoSeal™ bloks ir iepakots kopā ar dilatatoru un 0,038 collu (0,97 mm) OD, 27,5 collu (70 cm) garu vadītājstīgu un J taisnotāju; sk. tālāk **attēlu 1.3**. Vadītājstīga atrodas polietilēna caurulē. Visas daļas ir iepakotas fiksētā papīra paplātē. Iepakojumā ir arī pacienta implanta karte. FemoSeal™ Vascular Closure System, lai tā darbotos, kā paredzēts, nav nepieciešami papildu piederumi, un tā ir paredzēta lietošanai tikai ar dilatatoru un vadītājstīgu, kas iekļauta šī izstrādājuma iepakojumā.

Attēls 1.3. FemoSeal™ VCS bloks ar vadītājstīgu un dilatatoru



### 1.2.2 Izejvielas un komponenti

Zemāk 1.1. tabulā uzskaitīti FemoSeal™ VCS komponenti.

Tabula 1.1. FemoSeal™ VCS izejvielas un komponenti

| Daļas numurs | Apraksts                                                         |                                                                             | Materiāli                                                                                                                                                                                    |
|--------------|------------------------------------------------------------------|-----------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1            | 0,038 collu (0,97 mm) vadītājstīga ar vadītājstīgas J taisnotāju |                                                                             | Vadītājstīga: 304. kategorijas nerūsošais tērauds<br><br>J taisnotājs: polipropilēns, violets pigments<br><br>Skava: polietilēns<br><br>Caurulīte: polietilēns                               |
| 2            | FemoSeal dilatators                                              |                                                                             | Ligzda: tetrahidrofurāns, zils pigments, polibutilēna tereftalāts (PBT)<br><br>Caurulīte: liela blīvuma polietilēns (HDPE), melns pigments<br><br>Smērviela: silikons Dow Corning 360        |
| 3/4          | FemoSeal bloks                                                   | Pēc veidnes veidots RD7 — iekšējais blīvējums un ārējais bloķēšanas disks * | Kopolimērs starp glikolīdu, trimetilēna karbonātu, ε-kaprolaktonu un TMP: trimetilolpropānu (iniciators)                                                                                     |
|              |                                                                  | Daudzšķiedru serdenis *                                                     | Segmentēts kopolimērs starp L, L-laktīdu, trimetilēna karbonātu, ε-kaprolaktonu un 1,3 propanediolu (iniciatoru)<br><br>Pārklājums ir kopolimērs starp glikolīdu, ε-kaprolaktonu un L-lizīnu |

|  |  |                        |                                               |
|--|--|------------------------|-----------------------------------------------|
|  |  | Blietēšanas caurulīte  | Polipropilēns                                 |
|  |  | Stūmējs                | 304.V kategorijas nerūsošais tērauds          |
|  |  | Slīdnis                | Polibutilēntereftalāts (PBT)                  |
|  |  | Korpuss                | Polibutilēntereftalāts (PBT)                  |
|  |  | Poga                   | Polibutilēntereftalāts (PBT)                  |
|  |  | Pogas vāks             | Polioksimetilēns (POM)/poliacetāla kopolimērs |
|  |  | Uzmava                 | Polibutilēntereftalāts (PBT)                  |
|  |  | Starplika              | Polibutilēntereftalāts (PBT)                  |
|  |  | Konuss                 | Polipropilēns                                 |
|  |  | Korpusa vāks           | Polibutilēntereftalāts (PBT)                  |
|  |  | Drošības sprūds        | Polibutilēntereftalāts (PBT), zils pigments   |
|  |  | Uzmavas vāks           | Polibutilēntereftalāts (PBT)                  |
|  |  | Caurulītes blīve       | Silikona balsts A 70                          |
|  |  | Korpusa blīve          | Silikona balsts A 50                          |
|  |  | Atspere                | 302. kategorijas nerūsošais tērauds           |
|  |  | Konusa korpusa apvalks | Polipropilēns                                 |
|  |  |                        | Silikons Dow Corning 360, heksāns             |

\* Implantējamā ierīces daļa; implantējamie komponenti ir MR attēlveidošanas droši

FemoSeal™ VCS ir sterilizēta, izmantojot etilēna oksīdu (EO), un tā ir vienreizējai lietošanai paredzēta medicīniska ierīce. FemoSeal™ VCS ir veidota tā, lai to nevarētu izmantot atkārtoti.

### **Darbības veids**

FemoSeal™ VCS veicina mehānisku hemostāzi, izvietojot implantējamus slēgšanas elementus kopējā augšstilba artērijā un ārpus tās. Mehānismu, kas novērš asiņošanu, nodrošina iekšējais blīvējums, kas noblīvē punkcijas vietu, un ārējais bloķēšanas disks, kas notur iekšējo blīvējumu vietā.

### **1.2.3 Klīniskais ieguvums**

FemoSeal™ VCS nodrošina šādus klīniskos ieguvumus, salīdzinot ar asinsvadu slēgšanu pēc parastas augšstilba artērijas punkcijas:

- Mazāks laiks līdz hemostāzei<sup>1</sup>
- Mazāks laiks līdz brīdim, kad pacients var patstāvīgi pārvietoties<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heinford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

#### 1.2.4 Iepriekšējā(-ās) paaudze(-es) vai varianti

- FemoSeal™ VCS (Nr. 11200) pirmā versija tika pārdota Eiropas tirgū 2005. un daļēji 2006. gadā.
- Pašreizējā ierīce FemoSeal™ VCS (Nr. 11202) ar uzlabotu piegādes sistēmu tirgū ir pieejama kopš 2006. gada 28. marta.

#### 1.2.5 Piederumi, kas paredzēti lietošanai kopā ar šo ierīci

FemoSeal™ bloks ir iepakots kopā ar dilatatoru, 0,038 collu (0,97 mm) OD, 27,5 collu (70 cm) garu vadītārstīgu un J taisnotāju. Vadītārstīga ir FemoSeal™ bloka piederums. J taisnotājs ir vadītārstīgas komponents, savukārt dilatators ir FemoSeal™ bloka komponents. Vadītārstīga ir vienīgais vērā ņemamais piederums. Vadītārstīga atrodas polietilēna caurulē. Visas daļas ir iepakotas fiksētā papīra paplātē. Iepakojumā ir arī pacienta implanta karte. FemoSeal™ Vascular Closure System, lai tā darbotos, kā paredzēts, nav nepieciešami papildu piederumi, un tā ir paredzēta lietošanai tikai ar dilatatoru un vadītārstīgu, kas iekļauta šī izstrādājuma iepakojumā.

#### 1.2.6 Citas ierīces un izstrādājumi, kas paredzēti lietošanai kopā ar šo ierīci

Lai FemoSeal™ VCS darbotos, kā paredzēts, nav nepieciešamas papildu ierīces.

### 1.3 Riski un brīdinājumi

#### 1.3.1 Atlikušie riski un nevēlamas iedarbības

Zināmi vai paredzami nevēlamie notikumi, kaitējums un komplikācijas, kas saistītas ar ierīces FemoSeal™ VCS lietošanu, kā atlikušais risks ir uzskaitītas **tabulā 1.2**. Notikumu biežuma pamatā ir riska analīzes dokumentācija un aprēķini, pamatojoties uz pēcpārdošanas uzraudzības datiem no 2019. gada 1. septembra līdz 2024. gada 31. augustam. FemoSeal™ VCS nav nezināmu atlikušo risku, un visi attiecīgie riski ir novērsti, izmantojot lietošanas instrukcijas un risku pārvaldības procesu.



**Tabula 1.2. FemoSeal nevēlamie notikumi/komplikācijas**

| Kaitējums                                            | Sastopamība (%) | Mazinošie faktori                                                                                                                                              |
|------------------------------------------------------|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Alerģiska reakcija                                   | 0,0000          | Darbības un plāni maksimālai iespējamai risku mazināšanai ir risināti ar produkta dizaina iezīmēm, ražošanas vadlīnijām, produkta marķēšanu un ārstu apmācību. |
| Aneirisma                                            | 0,0000          |                                                                                                                                                                |
| AV fistula                                           | 0,0001          |                                                                                                                                                                |
| Asins zudums / asiņošana                             | 0,0280          |                                                                                                                                                                |
| Nāve                                                 | 0,0002          |                                                                                                                                                                |
| Ekhimoze                                             | 0,0000          |                                                                                                                                                                |
| Embolija                                             | 0,0000          |                                                                                                                                                                |
| Reakcija uz svešķermeni                              | 0,0000          |                                                                                                                                                                |
| Hematoma                                             | 0,0027          |                                                                                                                                                                |
| Asiņošana                                            | 0,0001          |                                                                                                                                                                |
| Infekcija                                            | 0,0002          |                                                                                                                                                                |
| Iekaisuma reakcija                                   | 0,0000          |                                                                                                                                                                |
| Nejutīgums                                           | 0,0000          |                                                                                                                                                                |
| Sāpes                                                | 0,0000          |                                                                                                                                                                |
| Pacienta diskomforts                                 | 0,0004          |                                                                                                                                                                |
| Procedūras aizkavēšana                               | 0,0065          |                                                                                                                                                                |
| Pseidoaneirisma                                      | 0,0004          |                                                                                                                                                                |
| Retroperitoneālā asiņošana                           | 0,0002          |                                                                                                                                                                |
| Sepse                                                | 0,0000          |                                                                                                                                                                |
| Trombembolija                                        | 0,0000          |                                                                                                                                                                |
| Tromboze                                             | 0,0001          |                                                                                                                                                                |
| Asinsvada oklūzija / apakšējās ekstremitātes išēmija | 0,0002          |                                                                                                                                                                |
| Asinsvada perforācija                                | 0,0000          |                                                                                                                                                                |
| Asinsvadu audu disekcija/lacerācija                  | 0,0003          |                                                                                                                                                                |

## 1.3.2 Brīdinājumi un piesardzības pasākumi

### Brīdinājumi

1. Nelietot, ja iepakojums ir bojāts vai ir bojāta sterilā barjera.
2. Nelietot pēc derīguma termiņa beigām — bioloģiski noārdāmie komponenti var pienācīgi nedarboties.
3. Nelietot, ja kādi priekšmeti izskatās bojāti vai ar kādiem defektiem.
4. Tādas FemoSeal™ Vascular Closure System lietošana, kurā var būt noticis bakteriāls procedūras apvalka vai apkārtējo audu piesārņojums, var izraisīt infekciju.
5. Ja ir aizdomas, ka aizmugurējā artērijas sienīņa ir pārdurta vai ir veikta vairāk nekā viena arteriālā punkcija, lai panāktu arteriālo hemostāzi, nepaļaujieties tikai uz FemoSeal™ Vascular Closure System vien. Izmantojiet papildu manuālo vai mehānisko kompresiju.
6. Ja punkcijas vieta atrodas augšstilba artērijā vai distālā virzienā no tās, FemoSeal™ Vascular Closure System nedrīkst lietot, jo pastāv risks, ka iekšējais blīvējums tiks novietots nepareizi. Šis notikums var izraisīt asiņošanas komplikācijas un/vai traucēt normālu asins plūsmu.
7. Ja incīzijas vietā ir nepārtraukta arteriāla asiņošana, nenogrieziet daudzšķiedru serdeni, līdz nav sasniegta hemostāze. Ja hemostāze netiek sasniegta, nostipriniet daudzšķiedru serdeni ar sterilu brūces pārsēju un nodrošiniet papildu kompresiju, līdz tiek sasniegta hemostāze. Nepārtrauktas arteriālās asiņošanas gadījumā var rasties ievērojamas asiņošanas komplikācijas, kas var izraisīt pacienta traumu vai nāvi.
8. Nelietojiet FemoSeal™ Vascular Closure System, ja punkcijas vieta ir proksimāla cirkšņa saitei, jo tas var izraisīt retroperitoneālu hematomu.
9. Pacientiem, kuriem ir augstāks asiņošanas risks, var rasties palielināts asins zudums un var būt nepieciešama asins pārliešana.
10. Ja iekšējais disks atdalās, tas var izraisīt trombotisku un/vai embolisku notikumu.

### Piesardzības pasākumi

1. FemoSeal™ Vascular Closure System izvietojšanas procedūra jāveic ārstiem, kas ir atbilstoši apmācīti par šīs ierīces lietošanu.
2. Pirms FemoSeal™ Vascular Closure System izvietojšanas veiciet ierobežotu femorālo angiogrammu vai ar ultraskaņu vadītu femorālo punkciju.
3. Pārtrauciet procedūru, ja:
  - kopējās augšstilba artērijas lūmena diametrs < 5 mm;

- parastās augšstilba artērijas punkcijas vietas tuvumā ir stenoze un/vai nozīmīgs iekaisuma plankums;
  - arteriālā punkcija ir augšstilba artērijas bifurkācijas vietā vai distāli no tās;
  - parastās augšstilba artērijas punkcijas vietas tuvumā ir anomāli atzarojumi vai asinsvadu anomālijas.
4. Ja ir kāda hematoma, lai konusa korpusa apvalku pareizi ievietotu artērijā, ir jāievēro īpaša piesardzība.
  5. Izmantojiet vienas sieniņas punkcijas metodi. Nepārduriet artērijas aizmugurējo sieniņu.
  6. Lietojot FemoSeal™ Vascular Closure System, vienmēr ievērojiet sterilitāti.
  7. FemoSeal™ Vascular Closure System ir paredzēta tikai vienreizējai lietošanai, un to nekādā veidā nedrīkst sterilizēt vai lietot atkārtoti. FemoSeal™ bloks ir veidots tā, lai to nevarētu izmantot atkārtoti.
  8. Ja iekšējā blīvējuma izvietošanas laikā ir jūtama neparedzēta pretestība, pārtrauciet procedūru.
  9. Lai pareizi izvietotu iekšējo blīvējumu, pārvietojiet īkšķi tā, lai poga varētu brīvi atlēkt atpakaļ.
  10. Pirms ārējā bloķēšanas diska izvietošanas pārliecinieties, vai FemoSeal™ bloka konusa korpusa apvalka gals atrodas zem ādas. Pacienti, kuriem ir neliels attālums starp femorālo artēriju un ādas līmeni, ārējais bloķēšanas disks var nejauši tikt izvietots virs ādas.
  11. Lai varētu ievietot pareizi, pirms ievietošanas var būt nepieciešams veikt iegriezumu ādā.
  12. Ja iekšējais blīvējums atrodas artērijā, bet nevar pilnībā nospiest pogu un izvietot ārējo bloķēšanas disku, var būt nepieciešama operācija, lai izņemtu FemoSeal™ slēgšanas elementus.
  13. Ja 18 mēnešu laikā ir nepieciešama atkārtota vienas un tās pašas augšstilba artērijas punkcija, atkārtota punkcija ir jāveic vismaz vienu centimetru proksimāli no iepriekšējās FemoSeal™ Vascular Closure System piekļuves vietas.
  14. Uzdodiet pacientam ievērot ārsta norādījumus par slēgšanas vietas pārbaudi.
  15. Norādiet pacientam nākamos 18 mēnešus nēsāt līdz pacienta informācijas karti

### **Piesardzības pasākumi izrakstīšanas laikā**

Pirms apsverat izrakstīšanu, novērtējiet šādus pacienta klīniskos apstākļus:

1. Asiņošana un/vai hematoma slēgšanas vietā.
2. Sāpes staigājot.
3. Infekcijas pazīmes slēgšanas vietā.

### 1.3.3 Drošības korigējošās darbības

Laika posmā no 2019. gada 1. septembra līdz 2024. gada 31. augustam tika veikta viena ar FemoSeal™ VCS saistīta drošības korigējošā darbība.

2022. gadā Terumo brīvprātīgi atsauca FemoSeal™ VCS, pamatojoties uz sūdzībām par kļūmēm Elkton ražotā FemoSeal produkta blietēšanas spēka mērīšanas un atvilkšanas spēka procesa un partijas izlaišanas testos. Kopumā tika atsaukti 950 bloki no Dienvidkorejas.

## 1.4 Klīniskais izvērtējums un pēcpārdošanas klīniskā novērošana

**1.3. tabulā** ir saraksts, kurā norādīti rakurspētījumi, kas veikti, laižot FemoSeal™ VCS tirgū, kā arī pēcpārdošanas pētījumi un pēcpārdošanas klīniskās novērošanas pasākumi. Pētījumā izmantotā ierīces versija ir iekļauta tālāk esošajā tabulā. FemoSeal™ VCS (Nr. 11200) pirmā versija bija pieejama tirgū līdz 2006. gadam, bet nākamā versija (Nr. C11202) tirgū tika laista 2006. gadā un ir pašlaik tirgū pieejamā versija.

### 1.3. tabula. Rakurspētījumu kopsavilkums

| Pirmspārdošanas funkcionālā testēšana ar dzīvniekiem                                                                                                                                                                                                                    | Ierīces versija               |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                         |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                         |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                         |
| Pirmais klīniskais pētījums ar cilvēkiem                                                                                                                                                                                                                                |                               |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                         |
| Pabeigti pēcpārdošanas klīniskie pētījumi                                                                                                                                                                                                                               |                               |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                                                                              | C11202<br>(pašreizējā ierīce) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                                                                                       | C11202<br>(pašreizējā ierīce) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                                                                                                                                                          | C11202<br>(pašreizējā ierīce) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)                                                                                                                                                  | C11202<br>(pašreizējā ierīce) |

| Plānotie/notiekošie pēcpārdošanas klīniskie pētījumi                                                                            |                               |
|---------------------------------------------------------------------------------------------------------------------------------|-------------------------------|
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                      | C11202<br>(pašreizējā ierīce) |
| Pēcpārdošanas klīniskās novērošanas pasākumi                                                                                    |                               |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(pašreizējā ierīce) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(pašreizējā ierīce) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(pašreizējā ierīce) |

### 1.4.1 Pirmspārdošanas pētījumu datu kopsavilkums (pētījumi ar dzīvniekiem un klīniskie pētījumi)

Tālāk esošajā **1.4. tabulā** ir aprakstīti visi pirmspārdošanas pētījumi ar dzīvniekiem un klīniskie pētījumi.

**1.4. tabula. Pirmspārdošanas pētījumu kopsavilkumi**

| Pirmspārdošanas funkcionālā testēšana ar dzīvniekiem                                                                                                                                                                                                                    |                                                                     |                                              |                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
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| Pētījuma nosaukums                                                                                                                                                                                                                                                      | Gads/CI                                                             | Pētījuma veids                               | Mērķis                                                                                                                                                                                                                                    | Nozīmīgākie punkti                                                                                                                                                                                                                                                                                                                                                                            | Iespējamie pieņemšanas kritēriji                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 2000<br><br>Radi Medical System AB<br><br>Veica Biomatech, Francija | Pētījums ar dzīvniekiem; izpētes izmeklējums | Pētījuma mērķis bija novērtēt tāda bionoārdamā implanta bioloģisko saderību un biofunktionalitāti, kas izstrādāts, lai panāktu hemostāzi asinsvadu sistēmā. Ziņojums par rezerves dzīvniekiem no pētījuma Nr. 862 (dokuments Nr. 1051-01) | <p>N = 3 pieaugušas aitu mātītes, 1 dzīvnieks katrā laika punktā</p> <p>Histopatoloģiskās analīzes, makroskopiskās gradācijas un ultrastrukturālās analīzes novērošana</p> <ul style="list-style-type: none"> <li>12 mēneši</li> <li>15 mēneši</li> <li>18 mēneši</li> </ul> <p>Krāsu doplerosonogrāfijas novērošana — 30 dienas miega artērijas un augšstilba artērijas piekļuves vietās</p> | <p>Arteriālā caurlaidība</p> <ul style="list-style-type: none"> <li>Asins plūsmas novērtējums pēc izvietošanas — 2/3 asins plūsmas samazināšanās, kas saistīta ar īslaicīgu arteriālo vazospazmu, kas tika attiecināta uz procedūru, abas šīs operācijas notika kreisajā kopējā miega artērijā</li> <li>Krāsu doplerosonogrāfijas izmeklējums (4 nedēļas) — 3/3 (100%) bez liela asins plūsmas samazinājuma 30 dienas pēc implantācijas</li> </ul> <p>Makroskopiskie novērojumi</p> <ul style="list-style-type: none"> <li>12 mēneši — caurlaidība makroskopiski apstiprināta, jo nav anatomiski redzamu</li> </ul> |

|                                                                  |                             |                          |                                                                    |                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
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|                                                                  |                             |                          |                                                                    |                                                                                                                 | <p>oklūziju; nav makroskopisku lokālu nepanesības bojājumu (asiņošana, nekroze vai neovaskularizācija); iekšējā diska iekapsulēšanās izskatījās marķēta</p> <ul style="list-style-type: none"> <li>15 mēneši — makroskopiskā novērošana neuzrādīja iekaisuma pazīmes; netika identificētas iekšējo un ārējo disku atliekas; iekapsulēšanas audi, kas atrodas ārējā diska apgabalā, izskatījās tāpat kā 12 mēnešu novērojumā</li> <li>18 mēneši — makroskopiskā novērošana neuzrādīja lokālas nepanesības pazīmes, ārējais disks ir redzams (3/3 gadījumi), iekšējā diska pilnīgas sadalīšanās; 1/3 (kreisā kopējā miega artērija) — artērijas sienīņas depresija implanta vietā (var būt saistīta ar ierīces izvietošanu)</li> </ul> <p>Secinājumi</p> <ul style="list-style-type: none"> <li>Makroskopiskos izmeklējumos 12, 15 un 18 mēnešus pēc implantācijas netika konstatētas nekrotiskas, deģeneratīvas vai trombotiskas pazīmes.</li> <li>Iekšējo un ārējo disku noārdīšanās process progresēja laikā no 12 līdz 18 mēnešiem, un, šķiet, tika pabeigts 18 mēnešu sasniegšanas laikā ar bālganiem audiem, kas pārklāj implantēto zonu.</li> <li>Histoloģiski pēc 18 mēnešiem polimēru materiāls vairs nebija redzams, bet bija endolumināli fibrozi audi. Netika novēroti nekrotiski, deģeneratīvi vai trombotiski bojājumi.</li> </ul> |
| Biocompatibility and Biofunctionality of a Biodegradable Implant | 2002 Radi Medical System AB | Pētījums ar dzīvniekiem; | Pētījuma mērķis bija novērtēt tāda bionoārdamā implanta bioloģisko | Novērošana (pēc implantācijas) <ul style="list-style-type: none"> <li>12 nedēļas</li> <li>24 nedēļas</li> </ul> | <u>Miega un augšstilba artērijas caurlaidība pēc 4 nedēļām</u>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |

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| to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | Veica Biomatech, Francija | izpētes izmeklējums | saderību, kas izstrādāts, lai panāktu hemostāzi asinsvadu sistēmā. | <ul style="list-style-type: none"> <li>36 nedēļas</li> </ul> <p>N = 12 aitas, 3 dzīvnieki katrā laika punktā, 3 rezerves dzīvnieki, kas nokauti pēc 12, 15 un 18 mēnešiem</p> <p>Implantācijas vietas — labās un kreisās puses augšstilba artērijas, labās un kreisās kopējāmiega artērija</p> <p>Krāsu doplerosonogrāfijas analīze</p> | <ul style="list-style-type: none"> <li>Liela asins plūsmas samazināšanās 0/12 (0%)</li> </ul> <p><u>Nav liela asins plūsmas samazināšanās</u></p> <ul style="list-style-type: none"> <li>Smagi asins plūsmas traucējumi, kas saistīti ar ierīces ievietošanu 0/12 (0%)</li> <li>Asins plūsmas samazināšanās kreisajā kopējā miega artērijā 2/12 (16,6%) pagaidu arteriālās vazospazmas dēļ (kas saistīta ar ķirurģiju, nevis ierīci)</li> </ul> <p><u>Asins plūsmas traucējumi saskaņā ar novērošanu</u></p> <p>12 nedēļas — 0/12 (0%)<br/>24 nedēļas — 0/12 (0%)<br/>36 nedēļas — 0/12 (0%)</p> <p>Asinsspiediena mērījumi (3 aitas — 36 nedēļas)</p> <ul style="list-style-type: none"> <li>Nav konstatēta liela asins plūsmas samazināšanās</li> </ul> <p>Makroskopiskie dati par integrāciju un noārdīšanos (0.–4. pakāpe)</p> <p><u>Miega artērijas vietas</u></p> <p><u>Iekšpuse</u></p> <p>-iekapsulēšanās<br/>12 nedēļas — 1,3<br/>24 nedēļas — 0,8<br/>36 nedēļas — 0,7</p> <p>-materiāla noārdīšanās<br/>12 nedēļas — 2,2<br/>24 nedēļas — 2,3<br/>36 nedēļas — 0,7</p> <p><u>Ārpuse</u></p> <p>-iekapsulēšanās<br/>12 nedēļas — 2,0<br/>24 nedēļas — 1,0<br/>36 nedēļas — 0,8</p> <p>-materiāla noārdīšanās<br/>12 nedēļas — 2,0<br/>24 nedēļas — 2,7</p> |
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|  |  |  |  |  | 36 nedēļas — 3,2<br><br><u>Augšstilba artērijas vietas</u><br><i>Ārpuse</i><br>-iekapsulēšanās<br>12 nedēļas — 1,0<br>24 nedēļas — 2,7<br>36 nedēļas — 1,0<br>-materiāla noārdīšanās<br>12 nedēļas — 2,0<br>24 nedēļas — 2,4<br>36 nedēļas — 3,0<br><br><i>Iekšpuse</i><br>-iekapsulēšanās<br>12 nedēļas — 2,0<br>24 nedēļas — 1,2<br>36 nedēļas — 1,0<br>-materiāla noārdīšanās<br>12 nedēļas — 1,0<br>24 nedēļas — 2,2<br>36 nedēļas — 3,0<br><br><u>Histoloģiskie dati par integrāciju, noārdīšanos un iekaisuma parametriem (atbilstošās vidējās vērtības, indekss 0–4) n=6</u><br><br><u>Miega artērijas vietas</u><br>Ārējā fibroze<br>12 nedēļas — 2,3<br>24 nedēļas — 2,3<br>36 nedēļas — 1,8<br>Iekšējā neointīma<br>12 nedēļas — 3,0<br>24 nedēļas — 2,7<br>36 nedēļas — 3,3<br>Materiāla noārdīšanās<br>12 nedēļas — 1,7<br>24 nedēļas — 3,0<br>36 nedēļas — 3 +<br>Iekaisuma parametri (makrofāgi)<br>12 nedēļas — 3,0<br>24 nedēļas — 1,7<br>36 nedēļas — 1,7<br><u>Augšstilba artērijas vietas</u><br>Ārējā fibroze<br>12 nedēļas — 1,3<br>24 nedēļas — 1,5 |
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|  |  |  |  |  | <p>36 nedēļas — 1,7</p> <p>Iekšējā neointīma</p> <p>12 nedēļas — 3,7</p> <p>24 nedēļas — 3,3</p> <p>36 nedēļas — 3,8</p> <p>Materiāla noārdīšanās</p> <p>12 nedēļas — 2,0</p> <p>24 nedēļas — 3,0</p> <p>36 nedēļas — 3+</p> <p>Iekaisuma parametri (makrofāgi)</p> <p>12 nedēļas — 3,5</p> <p>24 nedēļas — 1,8</p> <p>36 nedēļas — 1,8</p> <p><u>Histomorfoloģiskās caurlaidības vērtības</u></p> <p>Miega artērijas vietas</p> <p>12 nedēļas — 74,0%</p> <p>24 nedēļas — 81,9%</p> <p>36 nedēļas — 89,43%</p> <p>Augšstilba artērijas vietas</p> <p>12 nedēļas — 42,2%</p> <p>24 nedēļas — 73,21%</p> <p>36 nedēļas — 78,71%</p> <p><u>US asinsvadu caurlaidība (vidēji %)</u></p> <p>Miega artērijas vieta</p> <p>12 nedēļas — 94,6%</p> <p>24 nedēļas — 96,7%</p> <p>36 nedēļas — 94,7%</p> <p>Augšstilba artērijas vietas</p> <p>12 nedēļas — 66,9%</p> <p>24 nedēļas — 63,6%</p> <p>36 nedēļas — 75,1%</p> <p>Secinājumi</p> <ul style="list-style-type: none"> <li>• Netika konstatēta būtiska lokāla nepanesamība (nebija redzamu iekaisuma, nekrotisku vai deģeneratīvu bojājumu) pēc 12, 24 vai 36 nedēļām</li> <li>• Attiecībā uz saimniekorganismu un ierīci nav reģistrētas būtiskas nevēlamas audu reakcijas</li> <li>• Implanta noārdīšanās bija gandrīz pabeigta 36 nedēļu laikā</li> </ul> |
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| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002</p> <p>Radi Medical System AB</p> <p>Veica Biomatech, Francija</p> | <p>Pētījums ar dzīvniekiem</p> | <p>Pētījuma nolūks bija novērtēt tāda bionoārdamā implanta bioloģisko saderību un biofunktionalitāti, kas izstrādāts, lai panāktu hemostāzi asinsvadu sistēmā. Pārbaudītā ierīce bija paredzēta iekļūšanai artērijā pa punkcijas caurumu, lai panāktu hemostāzi. Viens disks tika ievadīts artērijā pa punkcijas caurumu, bet otrs nostiprināja iekšējo disku no artērijas ārpuses. Abi diski tika ievietoti caur ievadslūžas apvalku. Diski tika izstrādāti, lai novērstu asiņošanu, ieaugtu asinsvada sienā un visbeidzot noārdītos un uzsūktos. Pētījums bija paredzēts, lai savāktu un analizētu datus pēc funkcionālās implantācijas aitām un cūkām, lai novērtētu implanta spēju uzturēt fizioloģisko funkciju, ja to izmanto asinsrites sistēmā, lai noteiktu saimniekorganisma reakciju un ierīces reakciju (fizisko integritāti, audu iekapsulēšanos nokaušanas brīdī) un lai novērtētu implanta noārdīšanos</p> | <p>Implantācijas periods/novērošana visiem dzīvniekiem ir 5 nedēļas</p> <p>4 aitas, 1 cūka</p> <p>14 slēgšanas elementi</p> <p>8 slēgšanas elementi, kas implantēti 2 aitām,</p> <p>2 slēgšanas elementi, kas implantēti 1 cūkai</p> <p>Kad divi slēgšanas elementi tika implantēti vienā un tajā pašā augšstilba artērijā, tie tika implantēti attālumā &gt; 30 mm</p> | <p>Tika reģistrēti jebkādi nevēlamu pazīmju kritēriji (iekaisums, nekroze, asiņošana vai jebkādi citi bojājumi) vai jebkāda plāna pseidoīntīmas slāņa veidošanās. Īpaša uzmanība tika pievērsta ierīces sākotnējai integrācijai audos ar uzsvāru uz iekšējā diska iekapsulēšanos.</p> <p>Makroskopiski netika novērotas būtiskas lokālas nepanesības vai trombu veidošanās pazīmes. Makroskopiskā novērošana neatklāja nekādas atšķirības starp aitām vai cūku pēc augšstilba artērijās esošo slēgšanas elementu implantācijas.</p> <p>Makroskopiski netika novērotas būtiskas lokālas nepanesības vai trombu veidošanās pazīmes. Makroskopiskā novērošana neatklāja nekādas atšķirības starp aitām vai cūku pēc augšstilba artērijās esošo slēgšanas elementu implantācijas.</p> <p>Implantācijas vietas histopatoloģiskā analīze aitām neuzrādīja lokālas blakusparādības. Iekšējie un ārējie diski uzrādīja noārdīšanās pazīmes un dažos gadījumos bija salīzuši mazākās daļās. Iekšējie diski bija pilnībā integrēti jaunizveidotajos audos. Cūkai histopatoloģiskā analīze uzrādīja nelielu vairāk iekaisuma pazīmju ap</p> |
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|                                                                                                                                                                                                              |                              |                                                 |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                               | <p>iekšējiem un ārējiem diskkiem. Abu veidu dzīvniekiem daudzšķiedru serdenis uzrādīja nedaudz vairāk iekaisuma pazīmju nekā diska materiālā, kas ir normāli pītiem šuves diegiem lielākas virsmas platības dēļ.</p> <p>Asinsvada caurlaidība tika mērīta pēc 5 nedēļām, izmantojot trīs dažādas metodes, histomorfometrisko, histomorfometrisko kombinācijā ar asinsvada diametra mērīšanu, izmantojot bīdmēru un izmantojot krāsu doplera ultrasonogrāfiju. Vidējā asinsvadu caurlaidība aitām bija no 60 līdz 80% atkarībā no metodes (12 novērojumi). Cūkai vidējais asinsvadu caurlaidības līmenis bija no 40% līdz 80% (2 novērojumi).</p> |
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| <b>Pirmais klīniskais pētījums ar cilvēkiem</b>                                                                                                                                                              |                              |                                                 |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <b>Pētījuma nosaukums</b>                                                                                                                                                                                    | <b>Gads/CI</b>               | <b>Pētījuma veids</b>                           | <b>Mērķis</b>                                                                                                                                                                                                                                                                                 | <b>Nozīmīgākie punkti</b>                                                                                                                                                                                                                                                                                     | <b>Iespējamie pieņemšanas kritēriji</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Atklāts, vienas grupas, vairāku centru pētījums | Pētījuma mērķis bija noteikt FemoSeal Vascular Closure System (FemoSeal sistēma) kopumā un jo īpaši slēgšanas elementu drošumu, veikspēju un efektivitāti pacientiem, kam tiek veiktas sirds diagnostikas vai invazīvas kardioloģijas procedūras, izmantojot piekļuvi pa augšstilba artēriju. | <p>Pētījums 2 daļās</p> <p>Kopā n = 80</p> <p>1. daļas n = 20</p> <p>2. daļas n = 60</p> <p>Indikācijas:</p> <p>1. daļa — diagnostiska sirds katetrizācija, izmantojot augšstilba artēriju kā piekļuves vietu</p> <p>2. daļa — pacienti, kuriem tiek veiktas diagnostiskās un invazīvas sirds procedūras,</p> | <p>Rezultāti</p> <p><u>-hemostāze panākta ar FS bez kompresijas</u></p> <p>- 1. daļa 20/20 (100%)</p> <p>- 2. daļa 58/60 (97%)</p> <p>Vidējais hemostāzes laiks procedūras laikā (2. daļa) — 1,0 minūtes (tūlītējais diapazons — 8 minūtes)</p> <p><u>Laiks līdz brīdim, kad pacients var pastāvīgi pārvietoties (minūtes)</u></p> <p>1. daļa —</p>                                                                                                                                                                                                                                                                                              |

|  |  |  |  | izmantojot augšstilba artēriju kā<br>piekļuves vietu | Mediāna: 33,0<br>Vidēji: 67,8                                             |
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|  |  |  |  | 30 dienu novērošana                                  | 2. daļa —<br>Mediāna: 45<br>Vidēji: 87,5                                  |
|  |  |  |  |                                                      | <u>Smagu asinsvadu<br/>komplīkāciju rašanās —<br/>30 dienu novērošana</u> |
|  |  |  |  |                                                      | 1. daļa<br>-Nav asinsvadu<br>komplīkāciju 20/20<br>(100%)                 |
|  |  |  |  |                                                      | 2. daļa<br>Pseidoaneirisma — 1/59<br>(1,69%)                              |
|  |  |  |  |                                                      | <u>Nesekmīga ārstēšana</u>                                                |
|  |  |  |  |                                                      | 1. daļa — 0/20 (0%)                                                       |
|  |  |  |  |                                                      | 2. daļa — 3/60 (5%)                                                       |
|  |  |  |  |                                                      | • 2, jo neizdevās panākt<br>hemostāzi,<br>neizmantojot<br>kompresiju      |
|  |  |  |  |                                                      | • 1, jo radās lielas<br>asinsvadu<br>komplīkācijas,<br>pseidoaneirisma    |
|  |  |  |  |                                                      | <u>Pastāvīga sūce</u>                                                     |
|  |  |  |  |                                                      | 1. daļa — 0/20 (0%)                                                       |
|  |  |  |  |                                                      | 2. daļa — 8/60 (13%)                                                      |
|  |  |  |  |                                                      | <u>Hematoma</u>                                                           |
|  |  |  |  |                                                      | 1. daļa — 0/20 (0%)                                                       |
|  |  |  |  |                                                      | 2. daļa — 6/60 (10%)                                                      |

FemoSeal™ VCS pirmaspārdošanas attīstības plāna ietvaros tika veikti 3 funkcionālie testi ar dzīvniekiem. 2000. gadā pirms klīnisko pētījumu uzsākšanas tika veikts pētījums ar dzīvniekiem, lai novērtētu FemoSeal™ VCS biofunkcionalitāti. Šajā pētījumā tika novērtēta slēgšanas elementu spēja saglabāt fizioloģisko funkciju un novērtēta to noārdīšanās. Pēc 18 mēnešiem iekšējā un ārējā diska materiāls vairs nebija redzams, tas bija aizstāts ar endolumināliem

fibroziem audiem. Noslēgumā tika apstiprināta FemoSeal™ VCS noslēdzošā elementa spēja uzturēt fizioloģisko funkciju, ja to izmanto asinsrites sistēmā.

2002. gadā tika veikts pētījums, lai novērtētu bioloģiski noārdāma implanta FemoSeal™ VCS bioloģisko saderību un biofunktionalitāti, kas izstrādāts, lai panāktu hemostāzi asinsvadu sistēmā. Kopumā runājot, implanta noārdīšanās bija gandrīz pabeigta 36 nedēļās un nebija būtisku nevēlamu audu reakciju.

Citā pētījumā ar dzīvniekiem, kas tika veikts 2002. gadā, tika novērtēta tāda bionoārdāmā implanta FemoSeal™ VCS bioloģiskā saderība un biofunktionalitāte, kas izstrādāts, lai panāktu hemostāzi asinsvadu sistēmā. Pēc 5 nedēļām diska iekapsulēšana bija pabeigta un tika novērotas iekšējā un ārējā diska noārdīšanās pazīmes. Noslēgumā tika apstiprināta implanta spēja uzturēt fizioloģisko funkciju, ja to izmanto asinsrites sistēmā.

FemoSeal™ VCS klīniskās attīstības plāna ietvaros Radi Medical System AB veica pirmspārdošanas klīnisko pētījumu. Šis klīniskais pētījums nav publicēts vai pieejams tiešsaistē. Pētījums ar ierīces modeli nr. 11200 tika veikts 2002.–2004. gadā saskaņā ar Eiropas standartu EN 540 (Cilvēkiem paredzēto medicīnisko ierīču klīniskā izpēte) un saskaņā ar ICH vispārīgajiem apsvērumiem par klīniskajiem pētījumiem un labas klīniskās prakses vadlīnijām. Detalizēta informācija par šo pētījumu ir dokumentēta ziņojumā EU-SE-001. Šis klīniskais pētījums tika dokumentēts Radi Medical Systems AB beigu ziņojumā “Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures”. Šis klīniskais pētījums tika veikts ar FemoSeal™ pirmo modeli Nr. 11200, koncentrējoties uz implantējamo noslēgšanas komponentu drošumu un efektivitāti. Vienīgā atšķirība starp pirmo modeli Nr. 11200 un pašreizējo modeli C11202 ir izmērs pēc franču skalas — attiecīgi 6F un 7F – un uzlabota piegādes sistēma. Implantējamo noslēgšanas elementu, iekšējās blīves un ārējā bloķēšanas diska klīniskie ieguvumi, paredzētais lietojums, darbības principi un izejvielas paliek nemainīgi.

Ierīces paredzētais lietojums attiecas uz pacientiem, kam tiek veiktas diagnostiskas sirds vai invazīvas sirds procedūras, kā piekļuves punktu izmantojot augšstilba artēriju. Šī pētījuma mērķis bija noteikt FemoSeal™ VCS drošumu, veiktspēju un efektivitāti. Šis bija prospektīvs, vairāku centru, vienas grupas atklāts pētījums ar 30 dienu novērošanu.

Primārais veiktspējas mērķa kritērijs bija laiks hemostāzei, kas definēta kā straujas asiņošanas trūkums. Primārais drošības mērķa kritērijs bija lielu asinsvadu komplikāciju rašanās 30 dienu laikā. Sekundārie mērķa kritēriji ietvēra laiku līdz brīdim, kad pacients var patstāvīgi pārvietoties, ārstēšanas neveiksmju īpatsvaru, nevēlamu notikumu biežumu un ierīces veiktspējas raksturlielumus piegādes un izvietošanas laikā.

Šajā pētījumā iekļautie pacienti bija pieaugušie, kas varēja sniegt informētu piekrišanu un ar vismaz vienu neskartu apakšējo ekstremitāšu pulsu. Pacienti tika izslēgti no pētījuma, ja viņiem bija kāds no šiem nosacījumiem:

- perifēro asinsvadu slimību vēsture;
- autoimūna saslimšana;
- zināmi smagas anēmijas izraisīti asiņošanas traucējumi;
- INR >1,5;
- miokarda infarkts pēdējo 72 stundu laikā;
- nekontrolēta hipertensija, neskatoties uz ārstēšanu;
- aptaukošanās, kas izslēdz piekļuvi Seldingera tehnikai;
- asinsvadu transplantāta vai stenta klātbūtne arteriotomijas vietā;
- iepriekšēja ipsilaterāla punkcija pēdējo 3 mēnešu laikā;
- paredzamais mūža ilgums < 6 mēneši.

Turklāt pacienti tika izmeklēti operācijas laikā un izslēgti no pētījuma, ja tika novērota kāda no šīm pazīmēm:

- kopējās augšstilba artērijas lūmena diametrs <5 mm;
- arteriālie atzarojumi 2 cm attālumā proksimāli no punkcijas vietas;
- būtiska stenoze 3 cm attālumā no punkcijas vietas;
- primārā ievadslūžas apvalka lietošana >6 Fr;
- punkcija augšstilba artērijas bifurkācijas vietā vai distālajā daļā;
- vairākas augšstilba artērijas punkcijas;
- zināma vai iespējama augšstilba artērijas aizmugurējās sienas pārduršana;
- liela hematoma (2:6 cm) procedūras beigās;
- grūti ievadāma primārā apvalka procedūra likumotu audu vai asinsvada dēļ.

Šis vienprotokola pētījums tika veikts divās daļās: 1. daļā tika uzņemti 20 pacienti, pēc tam tika pabeigta drošības analīze, un pēc tam 2. daļā tika uzņemti vēl 60 pacienti.

1. daļā vidējais uzņemto pacientu vecums bija 65,9 gadi, 70,0% pacientu bija vīrieši un 95% pacientu līdztekus lietoja medikamentus. Pētījuma 2. daļā vidējais vecums bija 63,8 gadi, 78% bija vīrieši un 100% līdztekus lietoja medikamentus.

Pacientiem, kuriem veic diagnostiku (1. daļa un 2. daļa) vai invazīvās (2. daļa) sirds katetrizācijas procedūras, bija tiesības pretendēt uz uzņemšanu pētījumā. Šīs procedūras atbilda aprūpes standartam katrā iesaistītajā slimnīcā, kam sekoja FemoSeal™ VCS lietošana. Pacienta dati tika vākti sākumā, procedūras laikā, kā arī 1 dienu un 30 dienas pēc procedūras. Rezultāti ir

apkopoti **1.5. tabulā** un norāda, ka ierīce FemoSeal™ VCS ir droša un efektīva lietošanai šajā pacientu populācijā.

**Tabula 1.5. Pirmspārdošanas pētījumā paziņotie klīniskie rezultāti**

|                                                                                                                         | 1. daļa      | 2. daļa                   |
|-------------------------------------------------------------------------------------------------------------------------|--------------|---------------------------|
| Pacientu skaits                                                                                                         | 20           | 60                        |
| Vidējais laiks līdz hemostāzei                                                                                          | 1,2 minūtes  | 1,6 minūtes <sup>a</sup>  |
| Vidējais laiks līdz brīdim, kad pacients var patstāvīgi pārvietoties                                                    | 72,2 minūtes | 87,5 minūtes <sup>b</sup> |
| Lielu asinsvadu komplikāciju rašanās <sup>c</sup>                                                                       | 0 (0%)       | 1 (2%)                    |
| Pacientu skaits ar nevēlamajiem notikumiem                                                                              | 5 (25%)      | 19 (32%)                  |
| Ārstēšanas kļūme (definēta kā lielas asinsvadu komplikācijas, nepieciešamība pēc manuālas kompresijas vai abi gadījumi) | 0 (0%)       | 3 (5%)                    |
| Ierīces darbības traucējumi                                                                                             | 0 (0%)       | 6 (10%)                   |

<sup>a</sup> Pamatojoties uz kopējo parauga lielumu 58, jo iepriekšējo ipsilaterālo punkciju dēļ 2 pacienti procedūras laikā nerasniedza hemostāzi. Hemostāze šiem pacientiem tika sasniegta 7 minūtēs un 37 minūtēs.

<sup>b</sup> Pamatojoties uz kopējo parauga lielumu 59: 1 pacients netika iekļauts, jo tas tika pieslēgts ventilēšanai plaušu tūskas dēļ un nespēja patstāvīgi pārvietoties vairāk nekā nedēļu.

<sup>c</sup> Definēta kā ar asinsvadiem saistītas komplikācijas, kas prasa asins pārliešanu vai ķirurģisku labošanu, vai lokāla infekcija, kam nepieciešama antibiotiku lietošana, hospitalizācija vai hospitalizācijas laika pagarināšana, vai brūces tīrīšana

Pētījuma 1. daļā netika novērotas lielas asinsvadu komplikācijas. Pētījuma 2. daļā tika ziņots par vienu būtisku asinsvadu komplikāciju: pseidoaneirismu, par kuru ziņots vienas dienas laikā pēc procedūras. Šajā gadījumā bija nepieciešama ultraskaņas vadīta kompresija un trombīna injekcija pseidoaneirismā un ilgāka pacienta hospitalizācija.

No 5 nevēlamajiem notikumiem, par ko ziņots pētījuma 1. daļā, bija 1, iespējams, ar ierīci saistīts nevēlamais notikums: nebūtisks straujas asiņošanas gadījums 1 dienu pēc procedūras. No 19 nevēlamajiem notikumiem, par ko ziņots pētījuma 2. daļā, tika novēroti 3 ar ierīci saistīti nebūtiski nevēlami hematomas notikumi, un tika novēroti 6, iespējams, ar ierīci saistīti nebūtiski

notikumi, tostarp 3 ziņojumi par pastāvīgu sūci, 2 hematomām un 1 kāju sāpju gadījumu pēc vingrināšanas.

2. daļā tiek uzskatīts, ka ārstēšana bijusi nesekmīga 3 pacientiem: 2 sakarā ar nepanāktu hemostāzi, neizmantojot kompresiju, un 1 sakarā ar nopietnu asinsvadu komplikāciju (pseidoaneirismu). Pētījuma 1. daļā nesekmīga ārstēšana netika konstatēta.

No sešiem ierīces darbības traucējumiem pētījuma 2. daļā trīs netraucēja procedūru, viens bija saistīts ar lietotāja kļūdu, viens bija ievadslūžas noplūde, un viens bija salauzta šķiedru serdeņa locīkla. Pēdējās divas problēmas tika risinātas, izmantojot modeļu atjauninājumus, kas ieviesti modelī C11202.

Pirmspārdošanas klīniskā pētījuma 2. daļā netika ziņots par 6 mēnešu novērošanas rezultātiem, kas radušies pacienta neatbilstības dēļ. Pirmspārdošanas klīniskā pētījuma (EU-SE-001) 30 dienu rezultāti, kas atbilst klīniskajā dokumentācijā minētajam novērošanas laika periodam, pierāda, ka FemoSeal™ VCS ir droša un efektīva.

#### 1.4.2 Pirmspārdošanas klīnisko pētījumu datu kopsavilkums

Tālāk redzamajā **1.6. tabulā** ir aprakstīti 4 pabeigti pēcpārdošanas klīniskie pētījumi. Šie klīniskie pētījumi nav publicēti vai pieejami tiešsaistē.

**1.6. tabula. Pēcpārdošanas klīniskie pētījumi**

| Pabeigti pēcpārdošanas klīniskie pētījumi                                                   |                              |                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                        |
|---------------------------------------------------------------------------------------------|------------------------------|---------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|
| Pētījuma nosaukums                                                                          | Gads/CI                      | Pētījuma veids                                                      | Mērķis                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Nozīmīgākie punkti                                                                                                                                                                                                                                                                                                                        | Iespējamie pieņemšanas kritēriji                                                                                                       |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI                 | Pēcpārdošanas pētījums par to, kā lietotāji pieņem jauno iepakojumu | Pēcpārdošanas pētījums tika veikts par modeļa FemoSeal Vascular® Closure System Nr. 11202 atjauninājumu, kuram ir modificēta piegādes sistēma, salīdzinot ar pirmo modeli Nr. 11200, lai dokumentētu funkcionalitāti. Pētījuma mērķis bija saņemt atgriezenisko saiti par pārskatīto lietošanas pamācību (LP), ārstu un medmāsu apmācības projektu, apstiprināt riska analizē veiktos novērtējumus un sniegt ieguldījumu izstrādājuma kvalitātes uzlabošanā. | 100 pacienti <ul style="list-style-type: none"> <li>63 vīrieši/37 sievietes</li> <li>Vidējais vecums 68 gadi sievietēm, 65 gadi vīriešiem</li> </ul> 2 Zviedrijas slimnīcas, 6 ārsti<br><br>112 ierīces<br><br>Pacienta reģistrācijas veidlapās saglabātie dati (CRF)<br><br>Plānotais novērošanas laiks — 30 minūtes no lietošanas laika | Rezultāti<br><br>1. Ilustrācijas/instrukcijas LP tiek uzskatītas par informatīvām un atbilstošām<br><br>2. Tūlītēja hemostāze (91/100) |
| Confirmatory Assessment of FemoSeal™ Vascular                                               | Dr. Nikolasa Moesa Insbrukas | Pēcpārdošanas apstiprināšan                                         | Šī pētījuma mērķis bija novērtēt FemoSeal® drošumu un veiktspēju                                                                                                                                                                                                                                                                                                                                                                                             | 50 secīgi pacienti                                                                                                                                                                                                                                                                                                                        | Primārie mērķa kritēriji <ul style="list-style-type: none"> <li>Primārais efektivitātes mērķa kritērijs — TTH</li> </ul>               |



|                                                                                |                                  |                        |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                     |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|--------------------------------------------------------------------------------|----------------------------------|------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|-----|----------|-------|----------|-----------|----|----------|-----------|-------------------------|----------|--------------------|------------|---------------------|-----------|-------------------|---------|-----------------------|----------|--------------------------------|----------|----------------------|-----------|--------------------------|-----------|-----------------------------------|----------|----------------------|--------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Closure System in 7F-Sheath. (2008)                                            | medicīnas universitāte, Austrija | as novērtējums         | pacientiem, kuriem tika veikta diagnostiska sirds katetrizācija vai perkutāna sirds invazīva procedūra ar 7F apvalku.                                                                                                                                      | Indikācija — diagnostiska vai invazīva sirds katetrizācija no kopējās augšstilba artērijas<br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yr)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                                                                                                                                                                   | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yr) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | (laiks līdz hemostāzei) ar sūci vai bez tās, bet bez papildu manuālas vai mehāniskas kompresijas.<br>• Drošuma mērķa kritērijs — nevēlamo notikumu sastopamība — nelielas un lielas asinsvadu komplikācijas un visi citi nevēlamāie notikumi — nopietni un nebūtiski pētījuma laikā (t.i., līdz pacienta izrakstīšanai).<br><br>Rezultāti<br>• Vidējais laiks līdz hemostāzei<br>• Diagnostika — 56,6 ±29 sekundes<br>• Iejaukšanās 59,9 ±16,2 sekundes<br>• Visi pacienti 57,8 ±26,3<br>• Visi pacienti spēj patstāvīgi pārvietoties pēc 4 stundu gultas režīma bez nekādām problēmām.<br><br>Drošības rezultāti<br>• 49/50 (98%) bez asinsvadu komplikācijām līdz izrakstīšanai no slimnīcas<br>• Vidējais laiks līdz izrakstīšanai — 2,6 dienas<br>• 1/50 (2%) neliela asiņošana nākamajā dienā pēc mierīga mēģinājuma patstāvīgi pārvietoties dienā, kad veikta angiogrāfija |
| n                                                                              | 50                               |                        |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                     |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| men                                                                            | 35 (70%)                         |                        |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                     |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| women                                                                          | 15 (30%)                         |                        |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                     |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| PCI cases                                                                      | 15                               |                        |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                     |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| age (yr)                                                                       | 62.8±11.1                        |                        |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                     |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| body mass index (kg/m²)                                                        | 25.4±6.7                         |                        |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                     |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| systolic BP (mmHg)                                                             | 131.2±20.9                       |                        |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                     |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| diastolic BP (mmHg)                                                            | 77.9±10.6                        |                        |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                     |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| diabetes mellitus                                                              | 9 (18%)                          |                        |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                     |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| arterial hypertension                                                          | 34 (68%)                         |                        |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                     |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| previous coronary intervention                                                 | 13 (26%)                         |                        |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                     |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| preprocedure aspirin                                                           | 50 (100%)                        |                        |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                     |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| preprocedure clopidogrel                                                       | 50 (100%)                        |                        |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                     |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| Procedural unfractionated heparin                                              | 15 (30%)                         |                        |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                     |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| Procedural abciximab                                                           | 2 (4%)                           |                        |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                     |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009) | 2009 RADI                        | Pēcpārdošanas pētījums | Pētījumā būtu jāinformē, ja klientiem/lietotājiem ir bijušas problēmas ar jauno iepakojumu, jo īpaši nesterilo Tuvek/PET-PE maisiņa ārpusi.<br><br>Pētījumā arī jāsniedz informācija par to, vai ārstējošais ārsts ir manījis kādas atšķirības šīs ierīces | 25 ierīces<br>4 Zviedrijas slimnīcas<br><br>16/25 (64%) pacientu bija PCI pacienti, kuri lietoja stipras antikoagulācijas zāles                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Rezultāti<br>1. Ar iepakojumu saistītas problēmas — 21/25 (84%) gadījumos lietošana bija sekmīga; 4/25 (16%) gadījumos bija nesekmīga (1 jaunas ievadslūžas testēšana, 1 iekšējais disks, kad, veicot arteriotomiju atbalsta posmā, poga iznāca ārā un ārējais disks tika ievietots |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |

|                                                                                                                                        |                                        |                                                            |                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|----------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                        |                                        |                                                            | <p>lietošanas/izvietošanas posmos salīdzinājumā ar iepriekš izmantotajām ierīcēm.</p> <p>Pētījumā būtu jāsniedz arī informācija par jebkādam papildu vajadzībām saistībā ar izstrādājuma kvalitātes uzlabošanu.</p> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                | <p>griezuma audu kanālā, 2 tūlītēja hemostāze netika sasniegta, neskatoties uz to, ka izvietošanas problēmu nebija.)</p> <p>2. Tūlītēja hemostāze 19/25 (76%) pacientiem</p> <p>3. Asiņošana 11/25 (44%) — 9/25 (36%) sūce/asiņošana, 2/25 (8%) hematomas</p> <p>Kopējais notikumu skaits 19%</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <p>The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022)</p> | <p>2022/Terumo Medical Corporation</p> | <p>Prospektīvs, daudzcentru, novērojumu, pēcpārdošanas</p> | <p>Lai turpinātu demonstrēt FemoSeal™ VCS drošumu un efektivitāti, panākot kopējās augšstilba artērijas piekļuves vietu hemostāzi reāliem pacientiem, kam tiek veiktas perkutānas endovaskulāras procedūras.</p>    | <ul style="list-style-type: none"> <li>Pacienta novērošana pēc 30 dienām (<math>\pm</math> 7 dienas) ar slimnīcas vizīti vai tālruņa zvanu.</li> <li>Reģistrācija: 2021. gada decembris līdz 2022. gada jūlijs.</li> <li>230 reģistrēti pacienti, kuriem tiek veiktas diagnostiskas vai invazīvas endovaskulāras procedūras, kurās izmanto FemoSeal™.</li> </ul> <p>3 centri Eiropā: Francija (92 pacienti), Vācija (38 pacienti), Beļģija (100 pacienti).</p> | <ul style="list-style-type: none"> <li><b>Demogrāfiskie dati/blakusslimības:</b> <ul style="list-style-type: none"> <li>Dzimums: 161 vīrietis (70%)/69 sievietes 69 (30%).</li> <li>Vidējais vecums: <math>70 \pm 12</math>.</li> <li>ĶMI: <math>26,1 \pm 4,95</math> kg/m<sup>2</sup>.</li> <li>Hipertensija: 160 pacienti (69,6%).</li> <li>Dislipidēmija: 128 (55,7%).</li> <li>Koronāro artēriju slimība: 42 (18,3%).</li> <li>Aktīvs smēķētājs: 86 (37,6%).</li> <li>Iepriekš bijis smēķētājs: 66 (28,8%).</li> <li>Koronārā sirds slimība: 34 (14%).</li> <li>Iepriekšējs miokarda infarkts: 18 (7,8%).</li> <li>Perifēro artēriju revaskularizācija: 12 (5,2%) miega artērija un 83 (37,5%) un apakšējās ekstremitātes artērija.</li> <li>Prettrombocītu terapija (sākmstāvoklī): 211 (91,7%), tostarp 21 (9,1%) duālā prettrombocītu terapija (DAPT).</li> <li>Perorālu antikoagulantu lietošana: 40 (17,4%) pacientu.</li> </ul> </li> <li><b>Iejaukšanās raksturojums:</b> <ul style="list-style-type: none"> <li>Vieta: stacionārā klīnika 162 gadījumi (70,4%),</li> </ul> </li> </ul> |

|  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <p>ambulatorā klīnika 68 gadījumi (29,6%).</p> <p>- Dominējošā indikācija: kļaudikācija 147 gadījumi (63,9%).</p> <p>- Pieeja: 35 antegrāda (15,3%), 194 retrogrāda (84,7%).</p> <p>• <b>Primārie mērķa kritēriji:</b></p> <p>- Kombinētais drošuma (piekļuves vietas ekstremitātē nav nopietnu komplikāciju 6 stundu laikā pēc procedūras) un efektivitātes (sekmīga hemostāze punkcijas vietā) mērķa kritērijs tika sasniegts 215/226 (95,1%) [95% CI: 91,46; 97,55] pacientiem pilnas analīzes komplektā un 215/230 (93,5%) [95% CI 89,47, 96,30] pacientiem, kas ārstēti ar FemoSeal™ apstrādāto komplektu.</p> <p>- Efektivitātes mērķa kritērijs tika sasniegts 219/226 (96,9%) CI [93,7, 98,7] pacientiem.</p> <p>- Drošuma mērķa kritērijs sasniegts 220/230 (95,2%) [95% CI: 92,15, 97,90] pacientiem.</p> <p>• <b>Sekundārie mērķa kritēriji:</b></p> <p>- Nelielu komplikāciju neesamība piekļuves vietā sešas stundas pēc procedūras sasniegta 225/230 (97,8%) [95% CI: 95,00; 99,29].</p> <p>- Nopietnu un nelielu komplikāciju piekļuves vietā neesamība no sešām stundām līdz 30 dienām pēc procedūras sasniegta 219/230 (95,2%) [95% CI:91,60; 97,59] pacientiem.</p> <p>- Vidējais laiks līdz hemostāzei ar</p> |
|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

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|--|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <p>FemoSeal™ VCD: 0,42 (0,25; 0,50) minūtes.</p> <p>- Vidējais laiks līdz brīdim, kad pacients var patstāvīgi pārvietoties: 5,00 (4,54; 5,50) minūtes.</p> <p>- Vidējais slimnīcā uzturēšanās ilgums: 23,98 (22,72, 25,00) stundas.</p> <p>- FemoSeal™ VCS lietojamība: "viegli" vai "ļoti viegli" izvietot 98,7% gadījumos ("viegli" izvietot 21 (9,2%), "ļoti viegli" izvietot 205 (89,5%) gadījumos) ar nelielu pretestību vai bez pretestības izvietojšanas laikā 226 (98,3%) gadījumu.</p> <p>152/230 (66,1%) pacientu, kam veikta procedūra ar vadītājstīgu, kas iekļauta FemoSeal™ komplektā (GW 0,038") un ieteikta FemoSeal™, nebija ziņotu ierīces defektu vai nevēlamu notikumu.</p> |
|--|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

2006. gada pētījums tika veikts, lai apstiprinātu pašreizējās ierīces drošumu un efektivitāti ar uzlabotu piegādes sistēmu un saņemtu atgriezenisko saiti par FemoSeal™ VCS lietošanas instrukciju un apmācības programmu. Pētījumā tika iekļauti 100 pacienti, un primārais mērķa kritērijs bija tas, vai tika panākta hemostāze vai arī bija nepieciešama papildu manuāla vai mehāniska kompresija. Pētījumā secināts, ka lielākajā daļā gadījumu FemoSeal™ VCS lietošana bija sekmīga (91% panāca tūlītēju hemostāzi).

2008. gada pētījumā tika iekļauti 50 pacienti, lai novērtētu FemoSeal™ VCS drošumu un veikspēju, lietojot to parastās klīniskās rutīnas laikā pacientiem, kuriem tiek veikta sirds kateterizācija ar 7 Fr apvalku. Pētījuma primārais mērķa kritērijs bija apkopot datus par hemostāzi un laiku, līdz pacients var patstāvīgi staigāt bez papildu manuālas vai mehāniskas kompresijas. No pētījuma rezultātiem tika secināts, ka vidējais laiks līdz hemostāzei bija 57,8 sekundes, un visi pacienti spēja patstāvīgi staigāt pēc 4 stundu gultas režīma.

2009. gada pētījumā tika novērtēts jaunais FemoSeal™ VCS iepakojums. Pētījumā tika reģistrēti 25 pacienti. Primārais mērķa kritērijs bija tas, vai lietotājam radās problēmas ar iepakojumu.

Lietotāji neminēja nekādas problēmas saistībā ar jauno FemoSeal™ VCS iepakojumu. Šajā pētījumā tika apkopoti arī dati par laiku līdz hemostāzei.

2022. gada pētījuma mērķis bija perspektīvi ievākt datus par FemoSeal VCS drošumu un efektivitāti, lai panāktu kopējās augšstilba artērijas piekļuves vietu hemostāzi reāliem pacientiem, kam tiek veiktas perkutānas endovaskulāras procedūras. Pētījumā tika reģistrēti 230 pacienti. Primārie reģistra mērķa kritēriji ir procedūras sekmīgums (t.i., sekmīga punkcijas vietas hemostāze) un nozīmīgu komplikāciju (piem., asinsvadu traumu, asiņošanas piekļuves vietā, piekļuves vietas infekcijas, atkārtotas manuālas kompresijas un jaunu ar piekļuves vietu saistītas ipsilaterālas akūtas kāju išēmijas) samazināšana. Pētījumā secināts, ka FemoSeal™ VCS labi darbojas reālajā vidē un nodrošina efektīvu hemostāzi un zemu piekļuves vietas komplikāciju biežumu pacientiem, kuriem tiek veiktas perifērās endovaskulārās iejaukšanās. Tas pierāda labu veiktspēju ar īsu laiku līdz hemostāzei un labu atgriezenisko saiti operatoram, kas FemoSeal™ VCS padara par vērtīgu ierīci augšstilba piekļuves vietas slēgšanai.

### 1.4.3 Pēcpārdošanas klīniskās novērošanas datu kopsavilkums

#### 1.4.3.1 Pabeigta pēcpārdošanas klīniskā novērošana

Tālāk **1.7. tabulā** ir sniegts kopsavilkums par pabeigtajiem pēcpārdošanas klīniskās novērošanas pasākumiem.

**1.7. tabula. Pēcpārdošanas klīniskās novērošanas pasākumi**

| Pabeigti pēcpārdošanas klīniskās novērošanas pasākumi                     |             |                                                             |                                                                                                                                                                   |                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|---------------------------------------------------------------------------|-------------|-------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Pasākuma nosaukums                                                        | Gads/CI     | Pētījuma veids                                              | Mērķis                                                                                                                                                            | Nozīmīgākie punkti                                                                                                                                | Iespējamie pieņemšanas kritēriji                                                                                                                                                                                                                                                                                                                                                                                                                   |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021<br>TMC | Pēcpārdošanas klīniskā aptauja — augstas kvalitātes aptauja | Pēcpārdošanas aptauja, lai prospektīvi apkopotu atgriezenisko saiti par Eiropas Savienības tirgos izplatītās FemoSeal™ asinsvadu noslēgšanas ierīces izmantošanu. | <ul style="list-style-type: none"> <li>120 gadījumi</li> <li>8 unikāli ārsti ar &gt; 5 gadu pieredzi</li> <li>Vairākas Eiropas valstis</li> </ul> | <b>Ierīces novērtējumi no 1 līdz 5 — aptaujas ziņojumi</b> <ul style="list-style-type: none"> <li>Pieņemšanas kritēriji <ul style="list-style-type: none"> <li>Vērtējumi 3–5 tiek uzskatīti par labiem</li> <li>Visiem ziņojumiem jābūt ar <math>\geq 80\%</math> pozitīvām atsauksmēm</li> </ul> </li> <li>Rezultāti <ul style="list-style-type: none"> <li>Nav saņemts aptaujas paziņojums &gt; 20% ar negatīvām atbildēm</li> </ul> </li> </ul> |

| Pabeigti pēcpārdošanas klīniskās novērošanas pasākumi                                                                           |                  |                                                             |                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
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|                                                                                                                                 |                  |                                                             |                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                     | <ul style="list-style-type: none"> <li>○ Nav aizpildītas sūdzības par produktu</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                        |
| 20210298 – 0.035” and 0038” Guidewire Clinical Survey Report (2021)                                                             | 2021 TMC         | Pēcpārdošanas klīniskā aptauja — augstas kvalitātes aptauja | Pēcpārdošanas aptauja, lai prospektīvi apkopotu atgriezenisko saiti par Eiropas Savienības tirgos izplatītās 0,035 collu vadītājstīgas (iekļauta 6Fr Angio-Seal™ VIP asinsvadu noslēgšanas ierīces (VCD) komplektācijā) un 0,038 collu vadītājstīgas (iekļauta gan 8Fr Angio-Seal™ VIP VCD, gan FemoSeal asinsvadu noslēgšanas sistēmas komplektā) lietošanu. | <ul style="list-style-type: none"> <li>• Aptaujas par 0,035 collu stīgu <ul style="list-style-type: none"> <li>○ 106 aptaujas</li> <li>○ 64 ārsti</li> </ul> </li> <li>• Aptaujas par 0,038 collu stīgu <ul style="list-style-type: none"> <li>○ 109 aptaujas</li> <li>○ 55 ārsti</li> </ul> </li> <li>• 12 retrospektīvas aptaujas</li> </ul>      | <b>Ierīces novērtējumi no 1 līdz 5 — aptaujas ziņojumi</b> <ul style="list-style-type: none"> <li>• Pieņemšanas kritēriji <ul style="list-style-type: none"> <li>○ Vērtējumi 3–5 tiek uzskatīti par labiem</li> <li>○ Visiem ziņojumiem jābūt ar <math>\geq 80\%</math> pozitīvām atsauksmēm</li> </ul> </li> <li>• Rezultāti <ul style="list-style-type: none"> <li>○ Visas vadītājstīgas saņēma pieņemamus novērtējumus</li> <li>○ Nav iesniegtas sūdzības par produktu</li> </ul> </li> </ul> |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024 TMC/TE | Pēcpārdošanas klīniskā aptauja — augstas kvalitātes aptauja | Lai prospektīvi apkopotu atgriezenisko saiti par ES izplatīto FemoSeal VCS izmantošanu ar vadītājstīgām.                                                                                                                                                                                                                                                      | <ul style="list-style-type: none"> <li>• 126 aptaujas</li> <li>• 7 centri</li> <li>• 5 valstis</li> <li>• 2023. gada 14. novembris – 2024. gada 11. jūnijs</li> <li>• Ārsta medicīniskā specialitāte: <ul style="list-style-type: none"> <li>○ Asinsvadu ķirurģija</li> <li>○ Intervences radioloģija</li> <li>○ Angioloģija</li> </ul> </li> </ul> | <b>Ierīces novērtējumi 5 ballu skalā — aptaujas ziņojumi</b> <ul style="list-style-type: none"> <li>• Pieņemšanas kritēriji <ul style="list-style-type: none"> <li>○ Vērtējumi 3–5 tiek uzskatīti par labiem</li> <li>○ Visiem ziņojumiem jābūt ar <math>\geq 80\%</math> pozitīvām atsauksmēm</li> <li>○ Ja šajā aptaujā tiek norādīti nevēlami notikumi, tiem</li> </ul> </li> </ul>                                                                                                           |

| Pabeigti pēcpārdošanas klīniskās novērošanas pasākumi |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|-------------------------------------------------------|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                       |  |  |  |  | <div>ir jābūt tādiem, kādus paredzēja riska pārvaldība.</div> <ul style="list-style-type: none"> <li>Pacientu demogrāfiskie dati <ul style="list-style-type: none"> <li>Sievietes: 29,4% (37/126)</li> <li>Vīrieši: 69,8% (88/126)</li> <li>Dzimums nav norādīts: 0,8 (1/126)</li> <li>Vecums &gt;75 gadi: 31,7%</li> </ul> </li> <li>Rezultāti <ul style="list-style-type: none"> <li>Vadītājstīga, kas tiek piegādāta ar FemoSeal™ VCS: 101/126 (80,2%).</li> <li>Procedūras ilgums (minūtes): 63,4 (36,6) (vidējais (SD)); 57,0 (36,0-81,0) (vidējais (IQR))</li> <li>Visi FemoSeal™ VCS veikspējas novērtējumi bija labvēlīgi.</li> <li>Visi ar FemoSeal™ VCS piegādātās vadītājstīgas novērtējumi bija labvēlīgi.</li> <li>Viens (0,8%) nevēlams notikums: FemoSeal™ VCS diski nebija labi salāgoti,</li> </ul> </li> </ul> |

| Pabeigti pēcpārdošanas klīniskās novērošanas pasākumi |  |  |  |  |                                                                                                                                                                                      |
|-------------------------------------------------------|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                       |  |  |  |  | iespējams, tāpēc, ka tika izmantota stingra vadītājstīga (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 collas), kurai nepieciešama manuāla kompresija, lai panāktu hemostāzi. |

Terumo Medical Corporation pašreizējā ziņošanas periodā (no 2019. gada 1. septembra līdz 2024. gada 31. augustam) veica trīs ārstu lietotāju augstas kvalitātes aptaujas.

FemoSeal™ klīniskajos pētījumos tika apkopoti proaktīvi klīniskie dati par FemoSeal™ VCS drošumu un veikspēju klīniskās lietošanas laikā. Aptaujā tika iekļauti jautājumi par kopējo ierīci un ar to saistītajiem piederumiem, tostarp 0,038 collu vadītājstīgu un to tiešo mijiedarbību. Vadītājstīgas klīniskie pētījumi apkopoja proaktīvus klīniskos datus par drošumu un veikspēju, klīniski lietojot 0,038 collu vadītājstīgu, kas piegādāta ar FemoSeal™ VCS. Aptaujas jautājumi īpaši koncentrējās uz vadītājstīgas vispārēju izmantošanu, sākot ar ievadīšanu caur procedūras apvalku asinsvados un beidzot ar stieples izņemšanu.

FemoSeal™ VCS un 0,038 collu vadītājstīga, kas iekļauta ierīces komplektācijā, saņēma vērtējumus kā pieņemamas, un tika iesniegtas sešas (6) sūdzības par ierīci un deviņas (9) sūdzības par vadītājstīgu, pamatojoties uz augstas kvalitātes klīnisko aptauju sniegto komentāru novērtējumu. Gan par FemoSeal, gan vadītājstīgu sūdzības tika izvērtētas un izskatītas Terumo pēcpārdošanas uzraudzības procesa ietvaros. Netika konstatēti jauni riski vai riska līmeņi.

2024. gadā PMCF aktivitāšu ietvaros tika veikta ārstu lietotāju aptauja. Pētījuma rezultāti parādīja, ka FemoSeal™ VCS veikspējas novērtējums un drošums kopumā bija ļoti labvēlīgi. Ir pierādīta arī tādu citu vadītājstīgu saderība, kuras nav iekļautas standarta FemoSeal™ VCS komplektācijā.



### 1.4.3.2 Notiekošā/plānotā klīniskā pēcpārdošanas uzraudzība

TMC ir viena notiekošā/plānota pēcpārdošanas klīniskās novērošanas darbība. Tiks veikta klīniskā izpēte, lai prospektīvi apkopotu atgriezenisko saiti par vadītājstīgas izmantošanu ar ierīci FemoSeal VCS, kas izplatīta ES tirgū. Aptauju aizpildīs ārsti, lai pētījumā noskaidrotu, kuras vadītājstīgas viņi izmantoja procedūras laikā. Šīs aptaujas mērķis ir novērst nepilnību, kas identificēta kā literatūras un ārēju pārskatītāju komentāru trūkums par FemoSeal™ VCS saderību ar citu (nevis Terumo zīmolu) vadītājstīgu izmantošanu. Atgriezeniskā saite ietver tehniskos rezultātus, klīnisko veikspēju un drošumu, kas attiecas uz ierīces veikspēju ar citām vadītājstīgām.

### 1.4.4 Sistemātiskās literatūras pārskata datu kopsavilkums

Terumo Medical Corporation veic sistemātiskus literatūras apskatus, lai apkopotu un novērtētu klīniskā drošuma un veikspējas datus no publicētajiem pētījumiem par FemoSeal™ VCS un/vai līdzīgām ierīcēm. Publicētās literatūras ikgadējās pārbaudes mērķis ir identificēt iepriekš nezināmas blakusietekmes, novērot zināmas blakusietekmes, identificēt neparedzētus riskus un identificēt FemoSeal™ VCS iespējamu sistemātisku nepareizu lietošanu vai izmantošanu bez marķējuma.

Jaunākajā sistemātiskajā literatūras apskatā, kas aptver laikposmu no 2019. gada 1. septembra līdz 2024. gada 31. augustam, tika apzināti 29 publicēti pētījumi, kas sniedza klīniskā drošuma un veikspējas datus par FemoSeal™ VCS. Divdesmit trīs atsauksmes tika sniegtas par FemoSeal™ VCS lietošanu paredzētajam mērķim, bet par neparedzētu lietojumu tika ziņots deviņos pētījumos. Kopumā dokumentācijas apskatā par pētījumiem, kas attiecas uz FemoSeal™ VCS lietošanu, redzams, ka pētāmajā populācijā ir pārstāvēti tādi pacienti ES, kuriem tiek veiktas perkutānās vaskulārās katetrizācijas procedūras. Šo 23 recenzēto publikāciju par lietošanu paredzētajam mērķim sarakstu skatiet **3. sadaļā**.

Klīniskā veikspēja tika novērtēta šādā veidā:

- Laiks līdz hemostāzei ir īsāks par to laiku, kas ir nepieciešams jaunāko tehnoloģiju kopējās augšstilba artērijas perkutānai slēgšanai, vai tam līdzīgs.
- Laiks līdz spējai patstāvīgi pārvietoties ir īsāks par to laiku, kas ir nepieciešams jaunāko tehnoloģiju kopējās augšstilba artērijas perkutānai slēgšanai, vai tam līdzīgs.
- Pēcoperācijas komplikāciju biežums ir līdzīgs pašreizējiem aprūpes standartiem vai mazāks par tiem.

Pamatojoties uz šiem klīniskās veikspējas mērījumiem, šajā dokumentācijas pārskatā sniegtie dati parādīja, ka FemoSeal™ VCS var veiksmīgi izmantot augšstilba artērijas punkcijas (arteriotomijas) noslēgšanai pacientiem, kuriem veikta perkutāna katetrizācija, izmantojot 7 Fr vai mazāku procedūras apvalku. Pilnīga hemostāze tika sasniegta lielākajai daļai pacientu (79,65-100%), un vidējais laiks līdz hemostāzei bija 0,5 minūtes, vidējais laiks līdz izrakstīšanai

3 dienas. 69,2-86,7% pacientu spēja patstāvīgi staigāt pēc 5 stundām pēc slēgšanas, vidējais gultas režīma ilgums pēc operācijas bija 349 min. FemoSeal™ VCS kļūme tika novērota 3,68-4% gadījumu, un 0,9-4,4 % procedūru bija nepieciešama papildu manuāla kompresija.

Klīnisko drošumu novērtēja pēc nevēlamiem notikumiem, tostarp, bet ne tikai:

- Asiņošana
- Hematoma
- Pseudoaneirisma
- Zilums
- Arteriovenoza fistula
- Infekcija
- Nāve

Katram no šiem nevēlamajiem notikumiem ziņotais FemoSeal™ VCS sastopamības biežums iekļautajos pētījumos bija mazāks vai salīdzināms ar vēsturiski ziņoto līmeni manuālai kompresijai un citām asinsvadu slēgšanas ierīcēm.

Pārskatot 10 ziņojumus par gadījumiem, netika konstatēti nevēlami notikumi, jo netika konstatēti jauni, neparedzēti, negaidīti vai nepieņemami riski.

FemoSeal™ VCS lietošanas kopējā efektivitāte diagnostiskās angiogrāfijas vai invazīvo operāciju laikā ir atkarīga no vairākiem faktoriem, piemēram, dzimuma, vecuma, pacienta anatomijas, blakusslimībām, punkcijas vietas anatomiskā novietojuma, ķirurga pieredzes, VCD ievietošanas metodes, pēcoperācijas aprūpes u.c. Papildus tehniskajiem panākumiem, tostarp hemostāzes sasniegšanai, FemoSeal™ VCS nodrošināja klīniskos ieguvumus, kas saistīti ar asinsvadu slēgšanu pēc augšstilba artērijas punkcijas, piemēram, laika samazināšanos līdz hemostāzei, laika samazināšanos līdz patstāvīgai staigāšanai. FemoSeal™ VCS ierīču veikspējas iznākums atbilst iznākumam, kas sagaidāms šāda veida ierīcēm, ja tās tiek izmantotas paredzētajā veidā. Dažas atsauksmes, kas iegūtas pašreizējā meklēšanas periodā, parādīja, ka pētāmā ierīce tika izmantota anatomiskā vietā, kas nav kopējā augšstilba artērija, un arteriotomiju slēgšanai > 7 Fr, kas tiek uzskatīta par neparedzētu lietojumu.

Pārskatīšanas laikā netika konstatētas nezināmas blakusietekmes, negaidīti riski vai iespējama ierīces sistemātiska nepareiza lietošana. Tomēr, ja FemoSeal™ VCS piesardzīgi lieto apmācīti ārsti, medicīniskā ierīce darbojas kā noderīga un nepieciešama klīniskā ierīce. Kopumā mērķa terapija un līdz ar to FemoSeal™ VCS atbilst klīniskajām vajadzībām, kas pašlaik pastāv ar asinsvadu piekļuvi saistītu komplikāciju ārstēšanai.

Kopumā šajā dokumentācijas pārskatā sniegtajos datos netika konstatētas iepriekš nezināmas veikspējas vai drošuma problēmas klīniskajā vidē vai nelabvēlīga ietekme, kas radusies, pārsniedzot paredzamo/pieļaujamo līmeni. Tādēļ no šī dokumentācijas apskata var secināt, ka

FemoSeal™ VCS, kad to izmanto, lai nodrošinātu hemostāžu saspiešanu arteriotomijā pēc perkutānas kateterizācijas, turpina darboties, kā paredzēts, un nav saistīta ar nopietniem drošības notikumiem.

#### 1.4.5 Pēcpārdošanas uzraudzības datu kopsavilkums

Ir ieviesta proaktīva PMS sistēma, un visu sūdzību izskatīšana tiek veikta reizi mēnesī un saskaņā ar iekšējām ražošanas procedūrām. Tika analizēti sūdzību dati par laika periodu no 2019. gada 1. septembra līdz 2024. gada 31. augustam. Kopumā bija 28 medicīnisko ierīču kontroles (Medical Device Vigilance — MDV) ziņojumi un 476 klientu sūdzību ziņojumi ražotājam. No 28 MDV ziņojumiem 27 bija saistīti ar nelabvēlīgiem notikumiem un viens ar ierīces nepareizu darbību. Ziņošanas periodā bija divi nāves gadījumi, bet neviens no ziņotajiem nāves gadījumiem netika uzskatīts par saistītu ar pētāmo ierīci. Starp 476 sūdzībām, kas iesniegtas ražotājam, visbiežākie sūdzību iemesli bija izvietošanas grūtības (146 gadījumi, 0,0142% gadījumu). Otrs biežākais iemesls bija izvilksanas gadījumu kļūmju režīms — 0,0126% (130 notikumi).

FemoSeal™ Vascular Closure System ir pārdota vairāk nekā 1 030 136 eksemplāros visā pasaulē un 827 843 eksemplāros Eiropas Ekonomikas zonā. Aprēķinātais sūdzību biežums attiecībā pret globālajiem pārdošanas apjomiem ir 0,046%. Kopējais klientu sūdzību īpatsvars ir ļoti zems. Nav konstatēti jauni riski, kas nav iekļauti lietošanas pamācībā un riska dokumentācijā.

Nevēlamo blakusparādību sastopamības rādītāji ir norādīti **1.2. tabulā**. Sūdzībās netika identificēti jauni neparedzēti, pēkšņi vai nepieņemami riski. Zināmo nevēlamo blakusparādību biežums vai smagums būtiski nepalielinājās.

#### 1.4.6 Klīniskās veiktspējas un drošuma vispārīgs kopsavilkums

FemoSeal™ VCS ir indicēta lietošanai, lai slēgtu kopējās augšstilba artērijas punkciju (arteriotomiju) pacientiem, kam ir veikta perkutāna katetrizācija, izmantojot 7F (2,33 mm) vai mazāku procedūras apvalku. Šis klīniskais novērtējums ir balstīts uz pieejamo pirmspārdošanas un pēcpārdošanas klīnisko datu un tās literatūras visaptverošu analīzi, kas attiecas uz FemoSeal™ VCS paredzēto lietojumu.

Tika veikts visaptverošs pārskats par literatūru, kas publicēta laika posmā no 2019. gada 1. septembra līdz 2024. gada 31. augustam. Pierādījumu kopumā bija 29 pētījumi par FemoSeal™ VCS. Klīniskajā novērtējumā sniegtie pierādījumi ļauj secināt, ka, lietojot saskaņā ar indikācijām, pētāmā ierīce ir droša un efektīva, un jebkādi riski vai nevēlamās blakusparādības, kas var būt saistītas ar ierīci normālos lietošanas apstākļos, ir pieņemami riski, salīdzinot ar ieguvumiem pacientam. Pētāmo ierīču veiktspējas iznākums atbilst iznākumam, kas sagaidāms šāda veida ierīcēm, ja tās tiek izmantotas paredzētajā veidā.

Iespējamās nevēlamās blakusietekmes, kas saistītas ar FemoSeal™ VCS lietošanu, ietver nevēlamos notikumus, par ko parasti ziņo alternatīvu arteriotomijas slēgšanas līdzekļu

izmantošanas gadījumā, piemēram, asiņošanu un hematomu. Kopumā par FemoSeal™ VCS lietošanu ziņoto nevēlamo notikumu sastopamības rādītāji ir līdzīgi tiem, kas ziņoti par manuālās kompresijas un līdzīgu asinsvadu slēgšanas ierīču izmantošanas gadījumiem. Konkrēti runājot, asiņošanas un hematomas gadījumā ziņotie FemoSeal™ VCS rādītāji ir mazāki par ziņotajiem rādītājiem līdzīgām asinsvadu slēgšanas ierīcēm. Katrs no ziņotajiem nevēlamajiem notikumiem, gan no publicētās dokumentācijas, gan pēcpārdošanas uzraudzības, bija iepriekš konstatēti (sk. **sadaļu 1.3**).

Esošie FemoSeal VCS dati par klīnisko drošumu un veiktspēju liecina, ka šīs asinsvadu slēgšanas ierīces lietošana, ja tā notiek saskaņā ar lietošanas pamācību, pacientam sniedz ieguvumus, kas pārsniedz iespējamos riskus.

Kā norādīts iepriekšējās sadaļās, dati, kas sniegti par FemoSeal™ VCS, liecina par konsekvenci starp datiem, kas saistīti ar novērtējamo ierīci (piemēram, ierīces lietošana, drošības rezultāti, klīniskā veiktspēja un klīniskie ieguvumi), identificētajām ekvivalentajām ierīcēm un datiem, kas saistīti ar līdzīgām ierīcēm, kuras uzskaitītas pie jaunākajām tehnoloģijām.

Drošuma datu šķērsanalīzē netika konstatētas nepilnības starp tālāk norādīto:

- Datiem, kas minēti pie jaunākajām tehnoloģijām
- Novērtējamai ierīcei specifiskajiem datiem
- Datiem, kas minēti riska pārvaldības failā(-os)
- Marķējumā un/vai lietošanas instrukcijā minētos datos (t.i., atlikušie lietotājam nodotie riski tiek risināti).

Klīnisko drošumu pierāda zemie komplikāciju rādītāji, kas konstatēti publicētajā recenzētajā klīniskajā literatūrā, uzņēmuma sponsorētajos klīniskajos pētījumos, pēcpārdošanas datu pārskatos, kas saistīti ar neizņemšanu no pārdošanas. Nav konstatētas bažas par veiktspēju, pārskatīšanā izmantotajā literatūrā ir ietverts FemoSeal™ VCS lietojums, kas atbilst ražotāja paredzētajam lietojumam.

### **1.5. Iespējamās diagnostikas vai terapijas alternatīvas**

Manuālo kompresiju tradicionāli izmanto, lai panāktu hemostāzi arteriotomijas vietā pēc asinsvadu katetrizācijām. Manuāla kompresija ir saistīta ar pacienta imobilizāciju ilgu laiku (līdz 8 stundām pēc procedūras) un ar ievērojamu diskomfortu un ilgstošu uzturēšanos slimnīcā. Nesēnā sistemātiskā pārskatā tika konstatēts, ka vidējais laiks, lai panāktu hemostāzi ar manuālu kompresiju, bija 20,8 minūtes.<sup>1</sup>

Manuālas kompresijas alternatīvas ietver ārējas hemostatiskas ierīces, kas arteriotomijas vietā veic mehānisku kompresiju. Šīs ierīces nesaīsina laiku līdz hemostāzei vai laiku, lai brīdīm, kad pacients var patstāvīgi pārvietoties, bet samazina pieprasījumu pēc personāla, aizstājot manuālo

kompresiju ar mehānisku kompresiju. Ar mehāniskās kompresijas izmantošanu saistīto nevēlamo notikumu biežums ir līdzīgs notikumu biežumam ar manuālu kompresiju.

Asinsvadu slēgšanas ierīces, piemēram, FemoSeal™ VCS, ir paredzētas arteriotomijas noslēgšanai. To mērķis ir samazināt laiku līdz hemostāzei un nodrošināt agrāku spēju patstāvīgi pārvietoties. Nesenā sistemātiskā pārskatā, kurā bija ietvertas 13 komerciāli pieejamas ierīces, tika konstatēts, ka vidējais laiks līdz hemostāzei ar asinsvadu slēgšanas ierīci bija 5,4 minūtes. Vidējais hemostāzes laiks atsevišķām asinsvadu slēgšanas ierīcēm svārstījās no 1 minūtes (FemoSeal™ VCS) līdz 14 minūtēm; lielākajai daļai ierīču tas bija no 4 līdz 10 minūtēm.<sup>1</sup>

Bieži ziņotie nevēlamie notikumi, kas saistīti ar arteriotomijas vietas slēgšanu, ar manuālu kompresiju, ārējām hemostatiskām ierīcēm vai asinsvadu slēgšanas ierīcēm, ietver hematomu, asiņošanu piekļuves vietā, pseidoaneirismu, arteriovenoza fistulu un infekciju. Tajā pašā sistemātiskajā pārskatā (34 nejauši kontrolēti pētījumi, 14 401 pacients) tika konstatēts, ka nevēlamo notikumu biežums manuālās kompresijas un asinsvadu slēgšanas ierīču lietošanas gadījumos ir līdzīgs, izņemot to, ka asiņošanas rādītājs ar asinsvadu slēgšanas ierīcēm mēdz būt nedaudz augstāks.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heinford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Ieteiktais lietotāja profils un apmācība

FemoSeal™ Vascular Closure System paredzētie lietotāji ir ārsti, kuri ir apmācīti, lai viņi varētu veikt arteriālo piekļuvi un slēgšanu endovaskulārajās procedūrās, izmantojot kopējo augšstilba artēriju, un ir piedalījušies Terumo Medical Corporation FemoSeal™ ārstu instruēšanas programmā.

## 1.7 Attiecīgie saskaņotie un kopējie standarti

| Standarta<br>atsauce | Pašreizējais<br>atbilstības/<br>pārskatīšanas gads | Apraksts                                                                            |
|----------------------|----------------------------------------------------|-------------------------------------------------------------------------------------|
| ISO 11070            | 2014/AMD1:2018                                     | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1 |
| EN ISO 11070         | 2014/A1:2018                                       | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1 |

| Standarta<br>atsauce | Pašreizējais<br>atbilstības/<br>pārskatīšanas gads | Apraksts                                                                                                                                                                 |
|----------------------|----------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| FDA vadlīnijas       | 2021. gada<br>20. maijs                            | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                                                     |
| ASTM F2052           | 2015                                               | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment                                 |
| ASTM F2213           | 2017                                               | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment                                             |
| ASTM F2503           | 2020                                               | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                                                           |
| ASTM F2182           | 2019                                               | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging                                    |
| EN ISO 13485         | 2016/A11:2021                                      | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 13485            | 2016                                               | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 14644-1          | 2015                                               | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1       | 2015                                               | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2          | 2015                                               | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2       | 2015                                               | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of                                                                            |

| Standarta<br>atsauce  | Pašreizējais<br>atbilstības/<br>pārskatīšanas gads | Apraksts                                                                                                                                      |
|-----------------------|----------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
|                       |                                                    | cleanroom performance related to air cleanliness by particle concentration                                                                    |
| ISO 14644-3           | 2019                                               | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                      |
| EN ISO 14644-3        | 2019                                               | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                      |
| ISO 14698-1           | 2003                                               | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                         |
| EN ISO 14698-1        | 2003                                               | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                         |
| ISO 14698-2           | 2003/TC1:2004                                      | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| EN ISO 14698-2        | 2003/TC 1:2004                                     | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| USP <788>             | Nav piemērojams                                    | PARTICULATE MATTER IN INJECTIONS                                                                                                              |
| ES Farmakopeja 2.9.19 | Nav piemērojams                                    | Particulate Contamination: Sub-Visible Particles                                                                                              |
| IEC 62366-1           | 2015                                               | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN 62366-1            | 2015                                               | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN ISO 14971          | 2019/A11:2021                                      | Medical devices — Application of risk management to Medical devices                                                                           |
| ISO 14971             | 2019                                               | Medical devices — Application of risk management to Medical devices                                                                           |



| Standarta<br>atsauce | Pašreizējais<br>atbilstības/<br>pārskatīšanas gads | Apraksts                                                                                                             |
|----------------------|----------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| ASTM F1980           | 2016                                               | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1       | 2020                                               | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1          | 2018                                               | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2       | 2006                                               | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2          | 2006                                               | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3       | 2014                                               | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3          | 2014                                               | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4       | 2017                                               | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4          | 2017                                               | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| EN ISO 10993-5       | 2009                                               | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| ISO 10993-5          | 2009                                               | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| EN ISO 10993-6       | 2016                                               | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |
| ISO 10993-6          | 2016                                               | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |
| EN ISO 10993-10      | 15. maijs                                          | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                       |



| Standarta<br>atsauce | Pašreizējais<br>atbilstības/<br>pārskatīšanas gads | Apraksts                                                                                                                                         |
|----------------------|----------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-10         | 2021                                               | Biological evaluation of medical devices —Part 10:<br>Tests for irritation and skin sensitization                                                |
| EN ISO 10993-11      | 2018                                               | Biological evaluation of medical devices — Part 11:<br>Tests for systemic toxicity                                                               |
| ISO 10993-11         | 2017                                               | Biological evaluation of medical devices — Part 11:<br>Tests for systemic toxicity                                                               |
| EN ISO 10993-12      | 2021                                               | Biological evaluation of medical devices — Part 12:<br>Sample preparation and reference materials                                                |
| ISO 10993-12         | 2021                                               | Biological evaluation of medical devices — Part 12:<br>Sample preparation and reference materials                                                |
| EN ISO 10993-17      | 2009                                               | Biological evaluation of medical devices — Part 17:<br>Establishment of allowable limits for leachable<br>substances                             |
| ISO 10993-17         | 2002                                               | Biological evaluation of medical devices — Part 17:<br>Establishment of allowable limits for leachable<br>substances                             |
| ISO 10993-18         | 2020/A1:2022                                       | Biological evaluation of medical devices — Part 18:<br>Chemical characterization of medical device materials<br>within a risk management process |
| EN ISO 10993-18      | 2020/A1:2022                                       | Biological evaluation of medical devices — Part 18:<br>Chemical characterization of medical device materials<br>within a risk management process |
| EN ISO 10993-23      | 2021                                               | Biological evaluation of medical devices - Part 23:<br>Tests for irritation                                                                      |
| ISO 10993-23         | 2021                                               | Biological evaluation of medical devices - Part 23:<br>Tests for irritation                                                                      |
| ASTM F2382           | 2018                                               | Standard Test Method for Assessment of Circulating<br>Blood-Contacting Medical Device Materials on Partial<br>Thromboplastin Time (PTT)          |

| Standarta<br>atsauce | Pašreizējais<br>atbilstības/<br>pārskatīšanas gads | Apraksts                                                                                                                                                                     |
|----------------------|----------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F756            | 2017                                               | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>             | Nav piemērojams                                    | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>            | Nav piemērojams                                    | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI<br>ST72    | 2019                                               | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135         | 2014/A1:2019                                       | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135            | 2014/A1:2018                                       | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7       | 2008/A1:2022                                       | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |
| ISO 10993-7          | 2008/A1:2019                                       | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                                            |
| EN 556-1             | 2024                                               | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices              |
| EN ISO 11737-1       | 2018/A1:2021                                       | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                                        |
| ISO 11737-1          | 2018/A1:2021                                       | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                                        |

| Standarta<br>atsauce | Pašreizējais<br>atbilstības/<br>pārskatīšanas gads | Apraksts                                                                                                                                 |
|----------------------|----------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 11138-1       | 2017                                               | Sterilization of health care products - Biological indicators - Part 1: General requirements                                             |
| ISO 11138-1          | 2017                                               | Sterilization of health care products - Biological indicators - Part 1: General requirements                                             |
| EN ISO 11138-2       | 2017                                               | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| ISO 11138-2          | 2017                                               | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| EN ISO 15223-1       | 2016                                               | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| ISO 15223-1          | 2016                                               | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| EN 1041              | 2008/A1:2013                                       | Information supplied by the manufacturer of medical devices                                                                              |
| EN ISO 11607-1       | 2020/A1:2023                                       | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| ISO 11607-1          | 2019/A1:2023                                       | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| EN ISO 11607-2       | 2020/A1:2023                                       | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes       |
| ISO 11607-2          | 2019/A1:2023                                       | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes       |

| Standarta<br>atsauce | Pašreizējais<br>atbilstības/<br>pārskatīšanas gads | Apraksts                                                                                                                                                                           |
|----------------------|----------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM D4169           | 2016                                               | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                                       |
| ASTM F1886/F1886M    | 2016                                               | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                                |
| ASTM F2825           | 2018                                               | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                           |
| ASTM F2096           | 2011 (R 2019)                                      | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                                       |
| ASTM F88/F88M        | 2015                                               | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                               |
| MDCG 2021-24         | 2021                                               | Guidance on classification of medical devices                                                                                                                                      |
| MDCG 2020-3          | 2020                                               | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD         |
| MDCG 2020-8          | 2020                                               | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                                     |
| MDCG 2020-7          | 2020                                               | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                                  |
| MDCG 2020-6          | 2020                                               | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                               |
| MDCG 2019-9 v1       | 2022                                               | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                           |
| MDCG 2019-8 v2       | 2020                                               | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices |

| Standarta<br>atsauce | Pašreizējais<br>atbilstības/<br>pārskatīšanas gads | Apraksts                                                                                                                                                                                                                                                      |
|----------------------|----------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-15         | 2020                                               | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11         | 2021                                               | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19         | 2021                                               | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1<br>v4    | 2021                                               | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2          | 2019                                               | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1          | 2019                                               | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7          | 2018                                               | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6          | 2018                                               | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |
| MDCG 2018-4          | 2018                                               | MDCG 2018-4 Annex: UDI database Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                                                                                                  |
| MDCG 2018-3<br>v1    | 2020                                               | Guidance on UDI for systems and procedure packs                                                                                                                                                                                                               |
| MDCG 2021-25         | 2021                                               | Regulation (EU) 2017/745 - application of MDR requirements to ‘legacy devices’ and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC                                                                 |

| Standarta<br>atsauce   | Pašreizējais<br>atbilstības/<br>pārskatīšanas gads | Apraksts                                                                                                                     |
|------------------------|----------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|
| Meddev 2.12-2<br>Rev 2 | 2012                                               | Guidance document Medical devices - Market<br>surveillance - Post Market Clinical Follow-up studies -<br>MEDDEV 2.12/2 rev.2 |

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### 3.0 REDAKCIJU VĒSTURE

| SSCP redakcijas numurs      | Izdošanas datums        | Izmaiņu apraksts                                                              | Pilnvarotās iestādes apstiprināta redakcija                                                                                                                                                                                                                                                                                 |
|-----------------------------|-------------------------|-------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022                | 2023. gada 20. janvāris | Sākotnējais izdevums, pēc MDR CE sertifikācijas                               | <input checked="" type="checkbox"/> Jā<br>Apstiprināšanas valoda: English<br><input type="checkbox"/> Nē (attiecas tikai uz IIa vai dažām IIb klases implantējamām ierīcēm (MDR 52. panta 4. punkta 2. daļa), kurām pilnvarotā iestāde vēl nav apstiprinājusi SSCP)<br><input type="checkbox"/> Cits (norādiet):            |
| SSCP-FS-2023 — 1. redakcija | 2024. gada 15. marts    | Atjaunināts periodam no 2019. gada 1. janvāra līdz 2023. gada 31. decembrim.  | <input checked="" type="checkbox"/> Jā<br>Apstiprināšanas valoda: English<br><input type="checkbox"/> Nē (attiecas tikai uz IIa klases vai dažām IIb klases implantējamām ierīcēm (MDR 52. panta 4. punkta 2. rindkopa), kurām pilnvarotā iestāde vēl nav apstiprinājusi SSCP)<br><input type="checkbox"/> Cits (norādiet): |
| SSCP-FS-2024 1. redakcija   |                         | Atjaunināts periodam no 2019. gada 1. septembra līdz 2024. gada 31. augustam. | <input type="checkbox"/> Jā<br>Apstiprināšanas valoda: English<br><input type="checkbox"/> Nē (attiecas tikai uz IIa klases vai dažām IIb klases implantējamām ierīcēm (MDR 52. panta 4. punkta 2. rindkopa), kurām pilnvarotā iestāde vēl nav apstiprinājusi SSCP)<br><input type="checkbox"/> Cits (norādiet):            |

|                              |               |                                                                  |                                                                                                                                                                                                                                                                                                                                        |
|------------------------------|---------------|------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>2. redakcija | June 20, 2025 | Pārstrādāta, pamatojoties uz NSAI apstiprināšanas pieprasījumiem | <input checked="" type="checkbox"/> Jā<br>Apstiprināšanas valoda:<br>English<br><br><input type="checkbox"/> Nē (attiecas tikai uz IIa klases vai dažām IIb klases implantējamām ierīcēm (MDR 52. panta 4. punkta 2. rindkopa), kurām pilnvarotā iestāde vēl nav apstiprinājusi SSCP)<br><br><input type="checkbox"/> Cits (norādiet): |
|------------------------------|---------------|------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

**Saugos ir klinikinio veiksmingumo duomenų santrauka****Kraujagyslių uždarymo sistema  
FemoSeal™ Vascular Closure System**

|                                                                        |                                                                                               |
|------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| <b>Gamintojas</b>                                                      | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 JAV           |
| <b>Gamintojo unikalus registracijos numeris (SRN)</b>                  | US-MF-000019594                                                                               |
| <b>Vadovybės atstovas / asmuo, atsakingas už atitiktį reglamentams</b> | Kimberly Feitl<br>Vice President, kokybės užtikrinimo klausimai                               |
| <b>Bazinis UDI-DI</b>                                                  | 38970FS79                                                                                     |
| <b>EMDN numeris</b>                                                    | C900199 – hemostazės sistemos, kita                                                           |
| <b>Prietaiso klasė</b>                                                 | III klasė                                                                                     |
| <b>Metai, kai prietaisas buvo pirmą kartą pažymėtas CE ženklu</b>      | 2005                                                                                          |
| <b>ES atstovas</b>                                                     | Terumo Europe N.V.<br>Interleuvenlaan 40, 3001<br>Leuvenas<br>Belgija<br>SRN: BE-AR-000001433 |
| <b>Notifikuotoji įstaiga</b>                                           | NSAI<br>CE 0050                                                                               |

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Ši saugos ir klinikinio veiksmingumo duomenų santrauka (SKVDS) skirta visuomenei susipažinti su atnaujinta kraujagyslių uždarymo sistemos FemoSeal™ Vascular Closure System (VCS) pagrindinių saugos ir klinikinio veiksmingumo aspektų santrauka.

Toliau pateikiama naudotojams/sveikatos priežiūros specialistams skirta priemonės saugos ir klinikinio veiksmingumo santrauka **1.0 skyriuje**.

## **1.0 NAUDOTOJAMS/SVEIKATOS PRIEŽIŪROS SPECIALISTAMS SKIRTA SANTRAUKA**

SKVDS neskirta pakeisti naudojimo instrukciją, kuri yra pagrindinis dokumentas, užtikrinantis saugų prietaiso naudojimą, taip pat neskirta teikti diagnostinių ar terapinių pasiūlymų numatytiems naudotojams ar pacientams. SKVDS nėra skirta pakeisti privalomos implantų kortelių ar kituose privalomuose dokumentuose pateikiamos informacijos.

### **1.1 Numatytoji prietaiso paskirtis**

#### **1.1.1 Paskirtis**

Kraujagyslių uždarymo sistema FemoSeal™ Vascular Closure System yra medicinos priemonė, skirta arterinei punkcijai uždaryti po perkutaninio kateterizavimo per bendrąją šlaunies arteriją.

#### **1.1.2 Naudojimo indikacijos**

Kraujagyslių uždarymo sistema FemoSeal™ Vascular Closure System skirta naudoti uždarant bendrąją šlaunies arterinę punkciją (arteriotomiją) pacientams, kuriems buvo atliktas perkutaninis kateterizavimas naudojant 7F (2,33 mm) arba mažesnę procedūrinę movą.

#### **1.1.3 Kontraindikacijos ir (arba) apribojimai**

Kraujagyslių uždarymo sistemos FemoSeal™ Vascular Closure System negalima naudoti pacientams, kuriems atlikta arteriotomija, kurios metu naudojamos didesnės nei 7F (2,33 mm) movos ar įtaisai.

#### **1.1.4 Tikslinės pacientų populiacijos**

Kraujagyslių uždarymo sistemos FemoSeal™ Vascular Closure System saugumas ir veiksmingumas nustatytas 18 metų ir vyresniems pacientams, kuriems buvo atliktas perkutaninis kateterizavimas naudojant 7F (2,33 mm) arba mažesnę procedūrinę movą.

#### **1.1.5 Specialios pacientų populiacijos**

Kraujagyslių uždarymo sistemos FemoSeal™ Vascular Closure System saugumas ir veiksmingumas nebuvo nustatytas šioms pacientų populiacijoms:

- Pacientams, sergantiems autoimunine liga.
- Pacientams, kuriems atliekama terapinė trombolizė.
- Pacientams, sergantiems kliniškai reikšminga periferinių kraujagyslių liga.
- Pacientams su nekontroliuojama hipertenzija (>220 mmHg sistolinis arba >110 mmHg diastolinis).



- Pacientams, kuriems nustatytas kraujavimo sutrikimas, įskaitant trombocitopeniją (<100 000 trombocitų skaičius) arba anemiją (Hgb <10 mg/dl).
- Pacientams, kurių bendrosios šlaunies arterijos vidinis spindis mažesnis nei 5 mm.
- Pacientams, kurių sutrikusi inkstų ir (arba) kepenų funkcija.
- Pacientams, sergantiems kitomis atitinkamomis gretutinėmis ligomis.
- Populiacijai, turinčiai tam tikrą rasinę ir (arba) etninę kilmę.
- Pacientams, kuriems per 72 valandas pasireiškė miokardo infarktas.
- Pacientams, punkcijos vietoje turintiems kraujagyslių transplantatą arba stentą.
- Nėščioms arba žindančioms pacientėms.
- Jaunesniems nei 18 metų pacientams.

### 1.1.6 Numatytasis naudojimas

Kraujagyslių uždarymo sistemos FemoSeal™ Vascular Closure System numatytieji naudotojai yra gydytojai, turintys kvalifikaciją atlikti arterinę prieigą ir uždarymą atliekant endovaskulines procedūras per bendrąją šlaunies arteriją ir dalyvavę Terumo Medical Corporation FemoSeal™ gydytojų mokymo programoje.

## 1.2 Įtaiso aprašas

### 1.2.1 Įtaiso aprašas

Terumo Medical Corporation (TMC) pagaminta kraujagyslių uždarymo sistema FemoSeal™ Vascular Closure System – tai rezorbuojamasis kraujagyslių uždarymo įtaisas, skirtas pasiekti šlaunies arterijų hemostazę po perkutaninio kateterizavimo per bendrąją šlaunies arteriją.

FemoSeal™ uždarymo elementus sudaro du rezorbuojami polimeriniai diskai, vidinis sandariklis ir išorinis fiksavimo diskas, sutvirtinti rezorbuojamu daugiagysliu siūlu ir mechaniškai užsandarinantys arteriotomiją (žr. **1.1 pav.** ir **1.2 pav.**). Įvestas per kūginę korpuso movą, išorinis fiksavimo diskas prispaudžiamas prie daugiagyslio veleno, todėl mechaniškai užverinama punkcijos vieta tarp vidinio ir išorinio fiksavimo disko. Vidinis sandariklis ir išorinis fiksavimo diskas prilaikomi dėl daugiagyslio veleno trinties. Hemostazė pasiekama mechaninėmis priemonėmis. Uždarymo elementai suyra hidrolizės būdu.

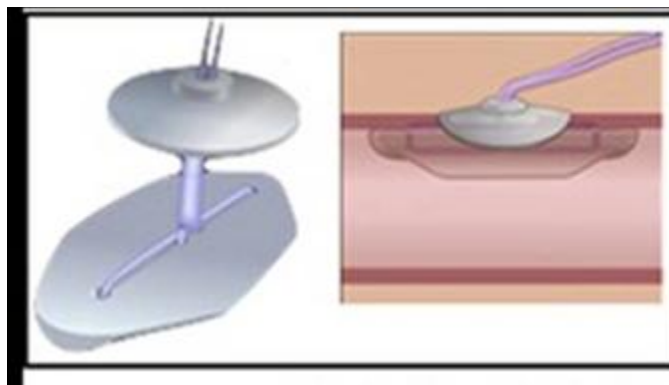
Implantuojami uždarymo komponentai, vidinis sandariklis ir išorinis fiksavimo diskas suyra per aštuoniolika (18) mėnesių, o daugiagyslis siūlas suyra ir hidrolizės būdu yra absorbuojamas aplinkinių audinių po dviejų (2) ar trejų (3) metų. Implantuojamų uždarymo komponentų gebėjimas išlaikyti arteriotomijos suspaudimą buvo išbandytas iki aštuonių (8) valandų. Yrantys

produktai metabolizuojami ir išsiskiria su šlapimu arba kaip anglies dioksidas pasišalina per plaučius. Tyrimų su gyvūnais metu kaupimosi poveikis nepastebėtas. Papildomi FemoSeal™ komponentai, kurie procedūros metu liečiasi su gyvais audiniais ar krauju, yra kūginė korpuso mova, plėtiklis, plėtimo vamzdelis, stūmiklis ir kreipiamoji viela.

### 1.1 pav. Atitinkamai vidinis sandariklis ir išorinis fiksavimo diskas

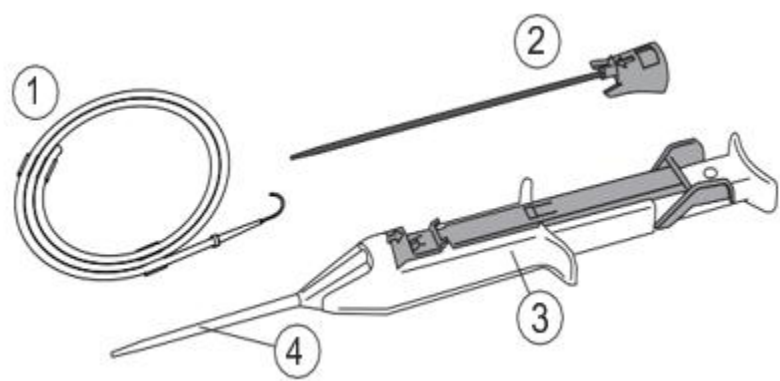


### 1.2 pav. Įvestas vidinis sandariklis ir išorinis fiksavimo diskas



FemoSeal™ įtaisas yra supakuotas kartu su plėtikliu ir 0,038 col. (0,97 mm) išorinio skersmens, 27,5 col. (70 cm) ilgio kreipiamąja viela ir J formos įtempikliu, žr. toliau pateiktą **1.3 pav.** Kreipiamoji viela yra polietileniniame vamzdelyje. Visos dalys supakuotos į fiksuotą popieriaus dėklą. Pakuotėje taip pat yra paciento implanto kortelė. Kad įtaisas veiktų kaip numatyta, kraujagyslių uždarymo sistemai FemoSeal™ Vascular Closure System nereikia papildomų priedų, o pats įtaisas yra skirtas naudoti tik su pakuotėje esančiu plėtikliu ir kreipiamąja viela.

Pav. 1.3 FemoSeal™ VCS įtaisas su kreipiamąja viela ir plėtikliu



1.2.2 Žaliavos ir komponentai

Toliau pateiktoje 1.1 lentelėje išvardyti FemoSeal™ VCS komponentai.

1.1 lentelė FemoSeal™ VCS medžiagos ir komponentai

| Dalies numeris | Aprašymas                                                     |                                                                   | Medžiagos                                                                                                                                                                                                        |
|----------------|---------------------------------------------------------------|-------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1              | 0,038 col. (0,97 mm) kreipiamoji viela su J formos įtempikliu |                                                                   | <p>Kreipiamoji viela: 304 Nerūdijantis plienas</p> <p>J formos įtempiklis: Polipropilenas, purpurinis pigmentas</p> <p>Spaustukas: polietilenas</p> <p>Vamzdelis: polietilenas</p>                               |
| 2              | FemoSeal™ plėtiklis                                           |                                                                   | <p>Įvorė: tetrahidrofuranas, mėlynas pigmentas, polibutileno tereftalatas (PBT)</p> <p>Vamzdelis: didelio tankio polietilenas (DTPE), juodas pigmentas</p> <p>Tepamoji priemonė: Silikonas „Dow Corning 360“</p> |
| 3/4            | FemoSeal™ įtaisas                                             | Formuotas RD7 – vidinis sandariklis ir išorinis fiksavimo diskas* | Kopolimeras tarp glikolido, trimetileno karbonato, ε-kaprolaktono ir TMP: trimetilpropanas (iniciatorius)                                                                                                        |
|                |                                                               | Daugiagyslis siūlas*                                              | Segmentuotas kopolimeras tarp L, L-laktido, trimetileno karbonato, ε-kaprolaktono ir 1,3 propanediolio (iniciatoriaus)                                                                                           |

|  |  |                     |                                                                  |
|--|--|---------------------|------------------------------------------------------------------|
|  |  |                     | Danga yra kopolimeras tarp glikolidų, ε-kaprolaktono ir L-lizino |
|  |  | Plėtimo vamzdelis   | Polipropilenas                                                   |
|  |  | Stūmiklis           | 304V nerūdijantis plienas                                        |
|  |  | Slankiklis          | Polibutileno tereftalatas (PBT)                                  |
|  |  | Korpusas            | Polibutileno tereftalatas (PBT)                                  |
|  |  | Mygtukas            | Polibutileno tereftalatas (PBT)                                  |
|  |  | Mygtuko dangtelis   | Polioksimetilenas (POM) / poliacetalo kopolimeras                |
|  |  | Mova                | Polibutileno tereftalatas (PBT)                                  |
|  |  | Tarpiklis           | Polibutileno tereftalatas (PBT)                                  |
|  |  | Kūgis               | Polipropilenas                                                   |
|  |  | Korpuso dangtis     | Polibutileno tereftalatas (PBT)                                  |
|  |  | Apsauginis įtaisas  | Polibutileno tereftalatas (PBT), mėlynas pigmentas               |
|  |  | Movos dangtelis     | Polibutileno tereftalatas (PBT)                                  |
|  |  | Vamzdelio tarpiklis | Silikoninė atrama A 70                                           |
|  |  | Korpuso tarpiklis   | Silikoninė atrama A 50                                           |
|  |  | Spyruoklė           | 302 nerūdijantis plienas                                         |
|  |  | Kūginė korpuso mova | Polipropilenas<br>Silikoninis „Dow Corning“ 360, heksanas        |

\*Implantuojama įtaiso dalis; implantuojami komponentai yra saugūs MRT aplinkoje

FemoSeal™ VCS yra sterilizuota etileno oksidu (EO) ir yra vienkartinio naudojimo medicinos priemonė. FemoSeal™ VCS įtaisas suprojektuotas taip, kad jo nebūtų galima naudoti pakartotinai.

### **Veikimo būdas**

FemoSeal™ VCS skatina mechaninę hemostazę, įterpiant implantuojamus uždarymo elementus į bendrąją šlaunies arteriją ir už jos ribų. Nuo kraujavimo apsaugantį mechanizmą užtikrina punkcijos vietą užsandarinantis vidinis sandariklis ir vidinį sandariklį prilaikantis išorinis fiksavimo diskas.

### 1.2.3 Klinikinė nauda

FemoSeal™ VCS teikia šią klinikinę naudą, susijusią su kraujagyslių uždarymu po bendrosios šlaunies arterijos punkcijos:

- Laiko iki hemostazės sutrumpinimas<sup>1</sup>
- Laiko iki ambuliacijos sutrumpinimas<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015).

*Sisteminis atsitiktinių imčių kontroliuojamų tyrimų, kuriuose lyginamas rankinis suspaudimas su kraujagyslių uždarymo prietaisais diagnostinėms ir terapinėms arterijų procedūroms, apžvalga. Tarptautinė chirurgijos technologija, 27, 32–44.*

### 1.2.4 Ankstesnė(-s) karta(-os) arba versijos

- Pirmoji FemoSeal™ VCS (Nr. 11200) versija Europos rinkoje buvo pardavinėjama 2005 ir 2006 metais.
- Dabartinė FemoSeal™ VCS (Nr. 11202) su patobulinta įvedimo sistema rinkoje pasiekama nuo 2006 m. kovo 28 d.

### 1.2.5 Kartu su įtaisu skirti naudoti priedai

FemoSeal™ įtaisas yra supakuotas kartu su plėtikliu, 0,038 col. (0,97 mm) išorinio skersmens, 27,5 col. (70 cm) ilgio kreipiamąja viela ir J formos įtempikliu. Kreipiamoji viela yra FemoSeal™ įtaiso priedas. J formos įtempiklis yra kreipiamosios vielos komponentas, o plėtiklis yra FemoSeal™ įtaiso komponentas. Kreipiamoji viela yra vienintelis reikalingas priedas. Kreipiamoji viela yra polietileniniame vamzdyje. Visos dalys supakuotos į fiksuotą popieriaus dėklą. Pakuotėje taip pat yra paciento implanto kortelė. Kad įtaisas veiktų kaip numatyta, kraujagyslių uždarymo sistemai FemoSeal™ Vascular Closure System nereikia papildomų priedų, o pats įtaisas yra skirtas naudoti tik su pakuotėje esančiu plėtikliu ir kreipiamąja viela.

### 1.2.6 Kartu su prietaisu skirti naudoti kiti įtaisai ir gaminiai

Kad veiktų kaip numatyta, FemoSeal™ VCS nereikia papildomų prietaisų.

## 1.3 Rizika ir Ispėjimai

### 1.3.1 Liekamoji rizika ir nepageidaujamas poveikis

Žinomi arba numatomi nepageidaujami reiškiniai, žala ir komplikacijos, susiję su FemoSeal™ VCS naudojimu dėl liekamosios rizikos, išvardyti **1.2 lentelėje**. Įvykių dažnis grindžiamas rizikos dokumentų analize ir apskaičiuojamas remiantis priežiūros po pateikimo į rinką duomenimis nuo 2019 m. rugsėjo 1 d. iki 2024 m. rugpjūčio 31 d. Nėra jokios nežinomos FemoSeal™ VCS liekamosios rizikos, o visos taikomos rizikos buvo pašalintos pateikus atitinkamas naudojimo instrukcijas.

**Lentelė 1.2. FemoSeal nepageidaujami reiškiniai/Komplikacijos**

| Žala                                              | Įvykio dažnis (%) | Lengvinantys veiksniai                                                                                                                                   |
|---------------------------------------------------|-------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| Alerginė reakcija                                 | 0,0000            | Rizikos mažinimo iki minimumo planai buvo sprendžiami atsižvelgiant į produkto dizaino ypatybes, gamybos gaires, produkto ženklinimą ir gydytojų mokymą. |
| Aneurizma                                         | 0,0000            |                                                                                                                                                          |
| AV fistulė                                        | 0,0001            |                                                                                                                                                          |
| Kraujo netekimas / kraujavimas                    | 0,0280            |                                                                                                                                                          |
| Mirtis                                            | 0,0002            |                                                                                                                                                          |
| Ekchimozė                                         | 0,0000            |                                                                                                                                                          |
| Embolija                                          | 0,0000            |                                                                                                                                                          |
| Reakcija į svetimkūnį                             | 0,0000            |                                                                                                                                                          |
| Hematoma                                          | 0,0027            |                                                                                                                                                          |
| Hemoragija                                        | 0,0001            |                                                                                                                                                          |
| Infekcija                                         | 0,0002            |                                                                                                                                                          |
| Uždegiminė reakcija                               | 0,0000            |                                                                                                                                                          |
| Tirpimas                                          | 0,0000            |                                                                                                                                                          |
| Skausmas                                          | 0,0000            |                                                                                                                                                          |
| Diskomfortas pacientui                            | 0,0004            |                                                                                                                                                          |
| Procedūros atidėjimas                             | 0,0065            |                                                                                                                                                          |
| Pseudoaneurizma                                   | 0,0004            |                                                                                                                                                          |
| Retroperitoninis kraujavimas                      | 0,0002            |                                                                                                                                                          |
| Sepsis                                            | 0,0000            |                                                                                                                                                          |
| Tromboembolija                                    | 0,0000            |                                                                                                                                                          |
| Trombozė                                          | 0,0001            |                                                                                                                                                          |
| Kraujagyslės okliuzija / apatinės galūnės išemija | 0,0002            | 0,0003                                                                                                                                                   |
| Kraujagyslės pradūrimas                           | 0,0000            |                                                                                                                                                          |
| Kraujagyslės audinio disekcija / įpjovimas        | 0,0003            |                                                                                                                                                          |

### 1.3.2 Įspėjimai ir atsargumo priemonės

#### Įspėjimai

1. Nenaudokite, jei pažeista pakuotė arba sterilus barjeras.
2. Nenaudokite pasibaigus tinkamumo laikui – biologiškai skaidūs komponentai gali tinkamai neveikti.
3. Nenaudokite, jei kurie nors elementai atrodo kaip nors pažeisti ar sugedę.
4. Naudojant kraujagyslių uždarymo sistemą FemoSeal™ Vascular Closure System, kai procedūrinė mova arba aplinkiniai audiniai gali būti užteršti bakterijomis, gali kilti infekcija.
5. Jei įtariama, kad galinė arterinė sienelė pradurta arba atlikta daugiau nei viena arterinė punkcija, norėdami pasiekti arterinę hemostazę nepasikliaukite vien kraujagyslių uždarymo sistema FemoSeal™ Vascular Closure System. Taikykite papildomą rankinį arba mechaninį suspaudimą.
6. Jei punkcijos vieta yra šlaunies arterijos išsišakojimo vietoje arba distalinėje jos dalyje, FemoSeal™ Vascular Closure System kraujagyslių uždarymo sistemos negalima naudoti, nes vidinis sandariklis gali būti įvedamas netinkamai. Šis įvykis gali sukelti kraujavimo komplikacijas ir (arba) sutrikdyti normalų kraujo tekėjimą.
7. Jei pjūvio vietoje yra nuolatinis arterinis kraujavimas, nenukirpkite daugiagyslio siūlo, kol nebus pasiekta hemostazė. Jei hemostazė nepasiekama, uždenkite daugiagyslį siūlą steriliu žaizdos tvarsčiu ir papildomai prispauskite, kol bus pasiekta hemostazė. Nuolatinio arterinio kraujavimo atveju galimos reikšmingos kraujavimo komplikacijos, dėl kurių pacientas gali būti sužalotas arba mirti.
8. Nenaudokite FemoSeal™ Vascular Closure System kraujagyslių uždarymo sistemos, jei punkcijos vieta yra proksimali kirkšnies raiščiui, nes tai gali sukelti retroperitoninę hematomą.
9. Pacientai, kuriems yra didesnė kraujavimo rizika, gali patirti didesnę kraujo netekimą, todėl gali prireikti kraujo perpylimo.
10. Atsikabinus vidiniam diskui, tai gali sukelti trombozinį ir (arba) embolinį įvykį.

#### Atsargumo priemonės

1. FemoSeal™ Vascular Closure System kraujagyslių uždarymo sistemos įvedimo procedūrą turi atlikti gydytojai, tinkamai apmokyti naudotis įtaisu.
2. Prieš įstatydami FemoSeal™ Vascular Closure System kraujagyslių uždarymo sistemą, atlikite ribotą šlaunies arterijos angiogramą arba ultragarsu valdomą šlaunies arterijos punkciją.

3. Nutraukite procedūrą, jei:
  - Bendrosios šlaunies arterijos spindžio skersmuo yra <5 mm.
  - Šalia bendrosios šlaunies arterijos punkcijos vietos yra stenoze ir (arba) reikšminga plokštelė.
  - Arterinė punkcija yra ties šlaunies arterijos išsišakojimu arba distalinėje dalyje.
  - Šalia bendrosios šlaunies arterijos punkcijos vietos yra anomalių šakų arba kraujagyslių anomalijų.
4. Jei yra hematoma, reikia būti ypač atsargiems, kad kūginė korpuso mova būtų tinkamai įstatyta į arteriją.
5. Naudokite vienos sienelės punkcijos techniką. Nepradurkite galinės arterijos sienelės.
6. Naudodami kraujagyslių uždarymo sistemą FemoSeal™ Vascular Closure System, visada laikykitės sterilumo reikalavimų.
7. FemoSeal™ Vascular Closure System kraujagyslių uždarymo sistema skirta naudoti tik vieną kartą, jos negalima sterilizuoti ar naudoti pakartotinai. FemoSeal™ įtaisas yra suprojektuotas taip, kad jo nebūtų galima naudoti pakartotinai.
8. Jei įvedant vidinį sandariklį netikėtai pajuntamas pasipriešinimas, procedūrą nutraukite.
9. Norėdami tinkamai įdėti vidinį sandariklį, uždėkite nykštį taip, kad mygtukas galėtų laisvai atšokti atgal.
10. Prieš įdėdami išorinį fiksavimo diską įsitikinkite, kad FemoSeal™ įtaiso kūginio korpuso movos galas yra po oda. Išorinis fiksavimo diskas gali būti netyčia įstatytas virš odos lygio pacientams, pas kuriuos atstumas tarp šlaunies arterijos ir odos lygio yra nedidelis.
11. Norint tinkamai įstatyti, prieš įvedant gali prireikti įpjauti odą.
12. Jei vidinis sandariklis yra arterijos viduje, tačiau neįmanoma iki galo nuspausti mygtuko ir įstatyti išorinio fiksavimo disko, FemoSeal™ uždarymo elementams pašalinti gali prireikti operacijos.
13. Jei per 18 mėnesių reikia atlikti tos pačios šlaunies arterijos punkciją, atlikite ją bent vienu centimetru proksimaliau ankstesnės FemoSeal™ Vascular Closure System kraujagyslių uždarymo sistemos prieigos vietos.
14. Informuokite pacientą apie poreikį laikytis gydytojo nurodymų dėl uždarymo vietos patikros.
15. Informuokite pacientą, kad kitus 18 mėnesių jis turės nešioti paciento informacinę kortelę



### Atsargumo priemonės išrašant

Prieš apsvarstydami išrašymą, įvertinkite šias paciento klinikoines būkles:

1. Kraujavimą ir (arba) hematomą uždarymo vietoje;
2. Skausmą vaikstant.
3. Uždarymo vietos infekcijos požymius.

### 1.3.3 Vietos saugos taisomieji veiksmai

Nuo 2019 m. rugsėjo 1 d. iki 2024 m. rugpjūčio 31 d. buvo atliktas vienas FemoSeal™ VCS saugos taisomasis veiksmas.

2022 m. Terumo savanoriškai atšaukė FemoSeal™ VCS dėl skundų, kur teigiama, kad Elkton gaminamo FemoSeal gaminio gamybos ir partijos išleidimo bandymai, skirti tamponavimo jėgos matavimui ir atitraukimo jėgai, buvo nesėkmingi. Iš viso Pietų Korėjoje buvo atšaukta 950 vienetų.

### 1.4 Klinikinio įvertinimo ir klinikinio stebėjimo po pateikimo rinkai santrauka

1.3 lentelėje pateikiamas pagrindinių tyrimų, skirtų FemoSeal™ VCS teikti rinkai, sąrašas, taip pat klinikiniai tyrimai po pateikimo į rinką ir klinikinio stebėjimo veikla po pateikimo į rinką. Tyrime naudojama įtaiso versija pateikta toliau esančioje lentelėje. Pirmoji FemoSeal™ VCS (Nr. 11200) versija buvo rinkoje iki 2006 m., kita versija (Nr. C11202) pateikta rinkai 2006 m. ir iki šiol joje yra.

1.3 lentelė. Pagrindinių tyrimų santrauka

| Funkcinis bandymas su gyvūnais prieš pateikiant rinkai                                                                                                                                                                                                                  | Įtaiso versija |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200          |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200          |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200          |
| Pirmasis klinikinis tyrimas su žmonėmis                                                                                                                                                                                                                                 |                |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200          |

| Po pateikimo į rinką atlikti klinikiniai tyrimai                                                                                |                               |
|---------------------------------------------------------------------------------------------------------------------------------|-------------------------------|
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                      | C11202<br>(esamas prietaisas) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                               | C11202<br>(esamas prietaisas) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | C11202<br>(esamas prietaisas) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)          | C11202<br>(esamas prietaisas) |
| Planuojami / vykdomi klinikiniai tyrimai po pateikimo rinkai                                                                    |                               |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                      | C11202<br>(esamas prietaisas) |
| Tolesnė klinikinė veikla po pateikimo rinkai                                                                                    |                               |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(esamas prietaisas) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(esamas prietaisas) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(esamas prietaisas) |

### 1.4.1 Duomenų iš tyrimų prieš pateikiant į rinką (bandymų su gyvūnais ir klinikinių tyrimų) santrauka

Toliau esančioje 1.4 lentelėje aprašomi visi iki pateikimo į rinką atlikti tyrimai, tiek su gyvūnais, tiek klinikiniai tyrimai.

1.4 lentelė. Tyrimų iki pateikimo į rinką santraukos

| Funkcinis bandymas su gyvūnais prieš pateikiant rinkai                                                             |                                |                                         |                                                                                                                                          |                                                                                                            |                                                                                                                                                                                 |
|--------------------------------------------------------------------------------------------------------------------|--------------------------------|-----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Tyrimo pavadinimas                                                                                                 | Metai / CI                     | Tyrimo tipas                            | Tikslai                                                                                                                                  | Etapai                                                                                                     | Galimi priėmimo kriterijai                                                                                                                                                      |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. | 2000<br>Radi Medical System AB | Tyrimas su gyvūnais; tiriamasis tyrimas | Tyrimo tikslas yra įvertinti biologiškai skaidaus implanto, skirto hemostazei kraujagyslių sistemoje pasiekti, biologinį suderinamumą ir | N = 3 suaugusios avys patelės, 1 gyvūnas per laikotarpį<br><br>Tolesni veiksmai histopatologinei analizei, | Arterinis pralaidumas<br>• Kraujo tėkmės įvertinimas po įvedimo – 2/3 kraujo tėkmės sumažėjimas, susijęs su laikinu arteriniu vazospazmu, kuris buvo priskirtas procedūrai, abu |

|                                                                                                                                                      |                               |  |                                                                                                            |                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
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| Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | Atlieka Biomatech, Prancūzija |  | biologinį funkcionalumą. Ataskaita skirta rezerviniams gyvūnams iš tyrimo Nr. 862 (dokumentas Nr. 1051-01) | makroskopiniam rūšiavimui ir ultrastruktūrinei analizei <ul style="list-style-type: none"> <li>• 12 mėn.</li> <li>• 15 mėn.</li> <li>• 18 mėn.</li> </ul> Spalvinio doplerio ultragarso stebėjimas – 30 dienų miego arterijose ir šlaunies arterijose | <div>įvyko kairiojoje bendrojoje miego arterijoje</div> <ul style="list-style-type: none"> <li>• Spalvinio doplerio ultragarso įvertinimas (4 savaitės) – 30 dienų po implantacijos 3/3 (100 %), be didelio kraujo srauto sumažėjimo</li> </ul> <div>Makroskopiniai stebėjimai</div> <ul style="list-style-type: none"> <li>• 12 mėn. – pralaidumas patvirtintas makroskopiškai, nes nėra anatomiškai matomos okliuzijos; nėra makroskopinių lokalaus netoleravimo pažeidimų (kraujavimas, nekrozė ar neovaskuliarizacija); buvo pažymėta vidinio disko inkapsuliacija</li> <li>• 15 mėn. – makroskopinis stebėjimas neparodė uždegimo požymių; nenustatyta vidinių ar išorinių diskų likučių; inkapsuliacijos audinys, esantis išorinio disko srityje, pasirodė taip pat, kaip 12 mėnesių stebėjimo metu</li> <li>• 18 mėn. – makroskopinis stebėjimas neparodė jokių vietinio netoleravimo požymių, matomas išorinis diskas (3/3 atvejų), pilnas vidinio disko degradavimas; 1/3 (kairioji bendroji miego arterija) – implantavimo vietoje stebimas arterijos sienelės suplonėjimas (gali būti susijusi su įtaiso įvedimu)</li> </ul> <div>Išvados</div> <ul style="list-style-type: none"> <li>• Praėjus 12, 15 ir 18 mėnesių po implantavimo, makroskopiniu būdu nebuvo nustatyta jokių nekrozinių, degeneracinių ar trombozinių požymių.</li> <li>• Vidinių ir išorinių diskų degradacijos procesas vyko nuo 12 iki 18 mėnesių ir atrodė baigtas po 18 mėnesių, su balkšvu audiniu, dengiančiu implantuotą sritį.</li> <li>• Histologiškai po 18 mėnesių polimerinė medžiaga nebebuvo</li> </ul> |
|------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|--|------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

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|                                                                                                                                                                                                                                                                         |                                                                      |                                         |                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                  | matoma, tačiau buvo aptiktas endoluminalinis pluoštinis audinys. Nenustatyta jokių nekrozinių, degeneracinių ar trombozinių pažeidimų.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 2002 m., Radi Medical System AB<br><br>Atlieka Biomatech, Prancūzija | Tyrimas su gyvūnais; tiriamasis tyrimas | Tyrimo tikslas yra įvertinti biologiškai skaidaus implanto, skirto hemostazei kraujagyslių sistemoje pasiekti, biologinį suderinamumą. | <p>Tolesni veiksmai (po implantacijos)</p> <ul style="list-style-type: none"> <li>• 12 sav.</li> <li>• 24 sav.</li> <li>• 36 sav.</li> </ul> <p>N = 12 avių, 3 gyvūnai per laikotarpį, 3 rezerviniai gyvūnai, paaugoti 12, 15 ir 18 mėnesiais</p> <p>Implantacijos vietos – dešinėsios ir kairiosios šlaunies arterijos, dešinėsios ir kairiosios bendrosios miego arterijos</p> <p>Spalvinis doplerio ultragarsinis tyrimas</p> | <p><u>Miego ir šlaunies arterijų pralaidumas po 4 savaitių</u></p> <ul style="list-style-type: none"> <li>• Didelis kraujo tėkmės sumažėjimas 0/12 (0 %)</li> </ul> <p><u>Neaptiktas didelis kraujo tėkmės sumažėjimas</u></p> <ul style="list-style-type: none"> <li>• Sunkus kraujo tėkmės sutrikimas, susijęs su įtaiso įvedimu 0/12 (0 %)</li> <li>• Kraujo tėkmės sumažėjimas kairiojoje bendrojoje miego arterijoje 2/12 (16,6 %) dėl laikino arterinio kraujagyslių spazmo (priskiriama operacijai, o ne įtaisui)</li> </ul> <p><u>Kraujo tėkmės sutrikimas tolesnio stebėjimo metu</u></p> <p>12 sav. – 0/12 (0 %)<br/>24 sav. – 0/12 (0 %)<br/>36 sav. – 0/12 (0 %)</p> <p>Kraujospūdžio matavimai (3 avys – 36 savaitės)</p> <ul style="list-style-type: none"> <li>• Neaptiktas didelis kraujo tėkmės sumažėjimas</li> </ul> <p>Makroskopiniai duomenys integracijai ir degradacijai (0–4 klasė)</p> <p><u>Miego arterijos vietos</u></p> <p><u>Vidinė pusė</u></p> <p>- inkapsuliacija</p> <p>12 sav. 1,3<br/>24 sav. 0,8<br/>36 sav. 0,7</p> <p>- medžiagos irimas</p> <p>12 sav. 2,2<br/>24 sav. 2,3<br/>36 sav. 0,7</p> <p><u>Išorinė pusė</u></p> <p>- inkapsuliacija</p> <p>12 sav. 2,0</p> |

|  |  |  |  |  | 24 sav. 1,0<br>36 sav. 0,8<br>- medžiagos irimas<br>12 sav. 2,0<br>24 sav. 2,7<br>36 sav. 3,2<br><br><u>Šlaunies arterijų vietos</u><br><u>Išorinė pusė</u><br>- inkapsuliacija<br>12 sav. 1,0<br>24 sav. 2,7<br>36 sav. 1,0<br>- medžiagos irimas<br>12 sav. 2,0<br>24 sav. 2,4<br>36 sav. 3,0<br><br><u>Vidinė pusė</u><br>- inkapsuliacija<br>12 sav. 2,0<br>24 sav. 1,2<br>36 sav. 1,0<br>- medžiagos irimas<br>12 sav. 1,0<br>24 sav. 2,2<br>36 sav. 3,0<br><br><u>Histologiniai integracijos,</u><br><u>degradacijos ir uždegiminių</u><br><u>parametrų duomenys</u><br><u>(atitinkamų verčių vidurkis,</u><br><u>indeksas 0–4) n=6</u><br><br><u>Miego arterijos vietos</u><br><u>Išorinė fibrozė</u><br>12 sav. – 2,3<br>24 sav. – 2,3<br>36 sav. – 1,8<br><u>Vidinis randas</u><br>12 sav. – 3,0<br>24 sav. – 2,7<br>36 sav. – 3,3<br><u>Medžiagos irimas</u><br>12 sav. – 1,7<br>24 sav. – 3,0<br>36 sav. – 3+<br><u>Uždegiminiai parametrai</u><br><u>(makrofagai)</u><br>12 sav. – 3,0<br>24 sav. – 1,7 |
|--|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | <p>36 sav. – 1,7</p> <p><u>Šlaunies arterijų vietos</u></p> <p>Išorinė fibrozė</p> <p>12 sav. – 1,3</p> <p>24 sav. – 1,5</p> <p>36 sav. – 1,7</p> <p>Vidinis randas</p> <p>12 sav. – 3,7</p> <p>24 sav. – 3,3</p> <p>36 sav. – 3,8</p> <p>Medžiagos irimas</p> <p>12 sav. – 2,0</p> <p>24 sav. – 3,0</p> <p>36 sav. – 3+</p> <p>Uždegiminiai parametrai (makrofagai)</p> <p>12 sav. – 3,5</p> <p>24 sav. – 1,8</p> <p>36 sav. – 1,8</p> <p><u>Histomorfologinio pralaidumo vertės</u></p> <p>Miego arterijos vietos</p> <p>12 sav. – 74,0 %</p> <p>24 sav. – 81,9 %</p> <p>36 sav. – 89,43 %</p> <p>Šlaunies arterijų vietos</p> <p>12 sav. – 42,2 %</p> <p>24 sav. – 73,21 %</p> <p>36 sav. – 78,71 %</p> <p><u>JAV kraujagyslių pralaidumas (vidutiniškai %)</u></p> <p>Miego arterijos pusė</p> <p>12 sav. – 94,6 %</p> <p>24 sav. – 96,7 %</p> <p>36 sav. – 94,7 %</p> <p>Šlaunies arterijų vietos</p> <p>12 sav. – 66,9 %</p> <p>24 sav. – 63,6 %</p> <p>36 sav. – 75,1 %</p> <p>Išvados</p> <ul style="list-style-type: none"> <li>Reikšmingas vietinis netoleravimo požymis (akivaizdžių uždegiminių, nekrozinų ar degeneracinių pažeidimų nebuvimas) 12–24 ar 36 sav. nenustatytas.</li> <li>Reikšmingos nepageidaujamos histologinės reakcijos,</li> </ul> |
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|                                                                                                                                                                                                                                                                        |                                                                               |                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                           | <p>susijusios su priimančiuoju ir įtaisu, nėra.</p> <ul style="list-style-type: none"> <li>Implanto degradacija buvo beveik baigta per 36 savaites</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002<br/>Radi Medical System AB<br/><br/>Atlieka Biomatech, Prancūzija</p> | <p>Tyrimas su gyvūnais</p> | <p>Tyrimo tikslas yra įvertinti biologiškai skaidaus implanto, skirto hemostazei kraujagyslių sistemoje pasiekti, biologinį suderinamumą ir biologinį funkcionalumą. Išbandytas įtaisas buvo skirtas įvesti į punkcijos vietą arterijoje, kad būtų pasiekta hemostazė. Vienas diskas įvedamas į punkcijos angą arterijoje, o kitas pritvirtina vidinį diską iš išorinės arterijos pusės. Abu diskai buvo įvesti per įleidiklio movą. Diskai yra sukurti taip, kad neleistų kraujuoti, sugytų kraujagyslės sienelėje ir galiausiai suirtų bei būtų absorbuoti. Tyrimas skirtas rinkti ir analizuoti duomenis po funkcinio implantavimo avims ir kiaulėms, siekiant įvertinti implanto gebėjimą palaikyti fiziologinę funkciją, kai jis naudojamas kraujotakos sistemoje, nustatyti priimančiojo atsaką ir įtaiso atsaką (fizinį vientisumą, histologinę inkapsuliaciją bandomajame gyvūne) ir įvertinti implanto irimą</p> | <p>Implantavimo laikotarpis / stebėjimas visiems gyvūnams 5 savaitės</p> <p>4 avys, 1 kiaulė</p> <p>14 uždarymo elementų</p> <p>8 uždarymo elementai, implantuoti į 2 avis,</p> <p>2 uždarymo elementai, implantuoti 1 kiaulei</p> <p>Kai du uždarymo elementai buvo implantuoti į tą pačią šlaunies arteriją, jie buvo implantuoti &gt;30 mm atstumu</p> | <p>Buvo registruojami bet kokie nepalankių požymių kriterijai (uždegimas, nekrozė, kraujavimas ar bet koks kitas pažeidimas) ar bet koks plonas pseudo-randinio sluoksnio susidarymas. Ypatingas dėmesys buvo skiriamas pradinei įtaiso histologinei integracijai, ypatingą dėmesį skiriant vidinei disko inkapsuliacijai.</p> <p>Makroskopiškai reikšmingų vietinio netoleravimo ar trombų susidarymo požymių nepastebėta. Makroskopinis stebėjimas neatskleidė jokio skirtumo tarp avių ar kiaulių po to, kai šlaunies arterijose buvo implantuoti uždarymo elementai. Makroskopiškai reikšmingų vietinio netoleravimo ar trombų susidarymo požymių nepastebėta. Makroskopinis stebėjimas neatskleidė jokio skirtumo tarp avių ar kiaulių po to, kai šlaunies arterijose buvo implantuoti uždarymo elementai.</p> <p>Avių implantavimo vietos histopatologinė analizė neparodė vietinių nepageidaujamų reakcijų. Vidiniuose ir išoriniuose diskuose buvo degradacijos požymių ir, kai kuriais atvejais, jie buvo suskaidyti į mažesnes dalis. Vidiniai diskai buvo visiškai</p> |

|                                                                                                                                                                                                              |                                  |                                              |                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                    | <p>integruoti į randinį audinį. Kiaulių histopatologinė analizė parodė šiek tiek daugiau uždegiminių požymių aplink vidinius ir išorinius diskus. Abiejuose gyvūnuose daugiagyslis siūlas sukėlė šiek tiek daugiau uždegimo požymių nei disko medžiaga, kas dėl didesnio paviršiaus ploto yra normalu pintiems siūlams.</p> <p>Kraujagyslės pralaidumas buvo matuojamas po 5 savaičių, naudojant tris skirtingus metodus: histomorfometrinių, histomorfometrinių ir kraujagyslių skersmens matavimą slankmačiu ir naudojant spalvinę doplerio ultragarsografiją. Vidutinis avių kraujagyslės pralaidumas buvo 60–80 %, priklausomai nuo metodo (12 stebėjimų). Kiaulių vidutinis kraujagyslės pralaidumas buvo 40–80 % (2 stebėjimai).</p> |
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| <b>Pirmasis klinikinis tyrimas su žmonėmis</b>                                                                                                                                                               |                                  |                                              |                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| <b>Tyrimo pavadinimas</b>                                                                                                                                                                                    | <b>Metai / CI</b>                | <b>Tyrimo tipas</b>                          | <b>Tikslai</b>                                                                                                                                                                                                                                                                          | <b>Etapai</b>                                                                                                                                                                                                                                                                                                      | <b>Galimi priėmimo kriterijai</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 m., Radi Medical Systems AB | Atviras, vienos grupės daugiacentris tyrimas | Tyrimo tikslai buvo nustatyti kraujagyslių uždarymo sistemos FemoSeal Vascular Closure System („FemoSeal System“), o konkrečiai – uždarymo elementų, saugumą, veiksmingumą ir efektyvumą pacientams, kuriems atliekamos širdies diagnostikos ar intervencinės kardiologinės procedūros, | <p>2 dalių tyrimas</p> <p>Iš viso n = 80</p> <p>1 dalis n = 20</p> <p>2 dalis n = 60</p> <p>Indikacijos:</p> <p>1 dalis – diagnostinis širdies kateterizavimas kaip prieigos vietą naudojant šlaunies arteriją</p> <p>2 dalis – pacientai, kuriems atliekamos diagnostinės ir intervencinės širdies procedūros</p> | <p>Rezultatai</p> <p><u>- hemostazė pasiekta su FS be suspaudimo</u></p> <p>- 1 dalis 20/20 (100 %)</p> <p>- 2 dalis 58/60 (97 %)</p> <p>Laiko mediana iki hemostazės procedūros metu (2 dalis) – 1,0 min. (tiesioginis intervalas – 8 minutės)</p> <p><u>Ambuliacijos laikas (minutėmis)</u></p> <p>1 dalis –</p>                                                                                                                                                                                                                                                                                                                                                                                                                         |



|  |  |  | naudojant šlaunies arterijos prieigą. | kaip prieigos vietą naudojant šlaunies arteriją | <p>Mediana: 33,0</p> <p>Vidut. reikšmė: 67,8</p> <p>2 dalis –</p> <p>30 dienų stebėjimas</p> <p>mediana: 45</p> <p>Vidut. reikšmė: 87,5</p> <p><u>Sunkių kraujagyslių komplikacijų dažnis – 30 dienų stebėjimas</u></p> <p>1 dalis</p> <p>- Be kraujagyslių komplikacijų 20/20 (100 %)</p> <p>2 dalis</p> <p>Pseudoaneurizma – 1/59 (1,69 %)</p> <p><u>Gydymo klaida</u></p> <p>1 dalis – 0/20 (0 %)</p> <p>2 dalis – 3/60 (5 %)</p> <ul style="list-style-type: none"> <li>• 2 dėl nepasiektos hemostazės nenaudojant suspaudimo</li> <li>• 1 dėl sunkių kraujagyslių komplikacijų, pseudoaneurizmos</li> </ul> <p><u>Nuolatinis kraujavimas</u></p> <p>1 dalis – 0/20 (0 %)</p> <p>2 dalis 8/60 (13 %)</p> <p><u>Hematoma</u></p> <p>1 dalis – 0/20 (0 %)</p> <p>2 dalis – 6/60 (10 %)</p> |
|--|--|--|---------------------------------------|-------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Įgyvendinant FemoSeal™ VCS vystymo iki pateikiant rinkai planą, buvo atlikti trys funkciniai bandymai su gyvūnais. Prieš pradėdant klinikinius tyrimus, FemoSeal™ VCS biologiniam funkcionalumui įvertinti 2000 m. buvo atliktas tyrimas su gyvūnais. Šiame tyrime įvertintas uždarymo elementų gebėjimas palaikyti fiziologinę funkciją ir įvertinti jų degradaciją. Po 18 mėnesių vidinė ir išorinė disko medžiaga nebebuvo matoma, pakeista endoliuminaliniu pluoštiniu audiniu. Apibendrinant buvo patvirtinta FemoSeal™ VCS uždarymo elemento geba fiziologinei funkcijai palaikyti, kai jis naudojamas kraujotakos sistemoje.

Siekiant įvertinti biologiškai skaidomo FemoSeal™ VCS implanto, skirto hemostazei kraujagyslių sistemoje pasiekti, biologinį suderinamumą ir biologinį funkcionalumą, 2002 m. buvo atliktas tyrimas su gyvūnais. Apibendrinant galima pasakyti, kad implantas beveik visiškai suiro per 36 savaites ir nebuvo reikšmingos nepageidaujamos audinių reakcijos.

Kito 2002 m. atlikto tyrimo su gyvūnais metu buvo įvertintas biologiškai skaidomo FemoSeal™ VCS implanto, skirto hemostazei kraujagyslių sistemoje pasiekti, biologinis suderinamumas ir biologinis funkcionalumas. Po 5 savaitžių disko inkapsuliacija buvo baigta ir buvo pastebėti vidinio ir išorinio diskų degradacijos požymiai. Apibendrinant, buvo patvirtintas implanto gebėjimas palaikyti fiziologinę funkciją, kai jis naudojamas kraujotakos sistemoje.

Pagal FemoSeal™ VCS klinikinės plėtros planą, prieš pateikiant rinkai, Radi Medical System AB atliko klinikinį tyrimą. Šis klinikinis tyrimas nėra skelbiamas arba pasiekiamas internete. Tyrimas su Nr. 11200 modelio įtaisu buvo atliktas 2002–2004 m. pagal Europos standartą EN 540 (medicininių prietaisų klinikinis tyrimas žmonėms) ir pagal ICH bendruosius klinikinių tyrimų reikalavimus ir geros klinikinės praktikos gaires. Išsami informacija apie šį tyrimą pateikta ataskaitoje EU-SE-001. Klinikinis tyrimas buvo aprašytas galutinėje Radi Medical Systems AB ataskaitoje „Multi-Centre Clinical Trial of the FemoSeal™ Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures“. Klinikinis tyrimas buvo atliktas naudojant pirmąjį FemoSeal modelį Nr. 11200 ir buvo sutelktas į implantuojamų uždarymo komponentų saugumą ir efektyvumą. Vienintelis skirtumas tarp pirmojo modelio Nr. 11200 ir dabartinio modelio C11202 yra prancūziški dydžiai, atitinkamai 6F ir 7F, ir patobulinta tiekimo sistema. Klinikinė nauda, numatytasis naudojimas, veikimo principai ir implantuojamų uždarymo elementų žaliavos, vidinis sandariklis ir išorinis fiksavimo diskas lieka nepakitę.

Įtaisas buvo skirtas pacientams, kuriems buvo atliekamos diagnostinės širdies ar intervencinės širdies procedūros, kaip prieigos tašką naudojant šlaunies arteriją. Šio tyrimo tikslas buvo nustatyti FemoSeal™ VCS saugumą, veiksmingumą ir efektyvumą. Tai buvo perspektyvinis, daugiacentris, vienos grupės atvirasis tyrimas su 30 dienų stebėjimu.

Pirminis veiksmingumo vertinamasis taškas buvo laikas iki hemostazės, apibrėžiamas kaip stipraus kraujavimo nebuvimas. Pirminė saugumo vertinamoji baigtis buvo sunkių kraujagyslių komplikacijų dažnis per 30 dienų. Antrinės vertinamosios baigtys apėmė laiką iki ambuliacijos,

gydymo sutrikimų dalį, nepageidaujamų reiškinių dažnį ir įtaiso veikimo charakteristikas įvedimo ir įdėjimo metu.

Į šį tyrimą įtraukti pacientai buvo suaugusieji, galintys pateikti informuoto asmens sutikimą ir turintys bent vieną nepažeistą apatinių galūnių pulsą. Pacientai nebuvo įtraukti į tyrimą, jei jie turėjo bet kurią iš šių būklių:

- Periferinių kraujagyslių ligų istoriją
- Autoimuninę ligą
- Žinomą sunkios anemijos kraujavimo sutrikimą
- INR >1,5
- Miokardo infarktą su 72 val.
- Nekontroliuojamą hipertenziją nepaisant gydymo
- Nutukimą, dėl kurio negalima prieiga taikant Seldingerio techniką
- Arteriotomijos vietoje yra kraujagyslių transplantatas arba stentas
- Ankstesnė ipsilateralinė punkcija 3 mėn. laikotarpyje
- Numatoma gyvavimo trukmė <6 mėn.

Be to, pacientai buvo tiriami operacijos metu ir neįtraukti į tyrimą, jei buvo pastebėta bet kuri iš šių būklių:

- Bendrosios šlaunies arterijos spindžio skersmuo <5 mm
- Arterinės šakos 2 cm diapazone iki punkcijos vietos
- Reikšminga stenoze 3 cm diapazone nuo punkcijos vietos
- Pirminės įleidiklio movos naudojimas >6Fr
- Punkcija ties šlaunies arterijos išsišakojimu arba distaline kryptimi
- Kelios šlaunies arterijos punkcijos
- Žinoma arba įtariama galinė šlaunies arterijos sienelės punkcija
- Didelė hematoma (2:6 cm) užbaigus procedūrą
- Dėl vingiuoto audinio ar kraujagyslės sunkus pirminės movos įvedimas procedūrai

Šis vieno protokolo tyrimas buvo atliktas dviem dalimis: 1 dalies metu buvo užregistruota 20 pacientų, tuomet atlikta saugos analizė, o 2 dalies metu užregistruota dar 60 pacientų.

1 dalyje vidutinis į tyrimą įtrauktų pacientų amžius buvo 65,9 m., 70,0 % pacientų buvo vyrai, 95 % pacientų tuo pat metu vartojo vaistus. Tyrimo 2 dalyje vidutinis amžius buvo 63,8 m., 78 % buvo vyrai ir 100 % pacientų tuo pat metu vartojo vaistus.

Į tyrimą galėjo būti įtraukti pacientai, kuriems buvo atliekama diagnostika (1 ir 2 dalys) arba intervencinės (2 dalis) širdies kateterizavimo procedūros. Procedūros atitiko kiekvienos tyrime dalyvavusios ligoninės priežiūros, kuri teikiama po FemoSeal™ VCS naudojimo, standartą. Pacientų duomenys buvo renkami tyrimo pradžioje, procedūros metu, 1 dieną ir 30 dienų po procedūros. Rezultatai apibendrinti **1.5 lentelėje** ir rodo, kad FemoSeal™ VCS yra saugu ir veiksminga naudoti šiai pacientų populiacijai.

**1.5 lentelė Klinikiniai rezultatai, gauti tyrimo metu prieš pateikiant į rinką**

|                                                                                                                             | 1 dalis   | 2 dalis                |
|-----------------------------------------------------------------------------------------------------------------------------|-----------|------------------------|
| Pacientų skaičius                                                                                                           | 20        | 60                     |
| Vidutinis laikas iki hemostazės                                                                                             | 1,2 min.  | 1,6 min. <sup>a</sup>  |
| Vidutinis laikas ambuliacijai                                                                                               | 72,2 min. | 87,5 min. <sup>b</sup> |
| Sunkių kraujagyslių komplikacijų dažnis <sup>c</sup>                                                                        | 0 (0 %)   | 1 (2 %)                |
| Pacientų, kuriems pasireiškia nepageidaujami reiškiniai, skaičius                                                           | 5 (25 %)  | 19 (32 %)              |
| Gydymo nepakankamumas (apibrėžiamas kaip pagrindinės kraujagyslių komplikacijos, poreikis suspausti rankiniu būdu arba abu) | 0 (0 %)   | 3 (5 %)                |
| Įtaiso gedimai                                                                                                              | 0 (0 %)   | 6 (10 %)               |

<sup>a</sup>Remiantis bendru imties dydžiu 58, nes 2 pacientai procedūros metu nepasiekė hemostazės dėl ankstesnės ipsilateralinės punkcijos. Šiems pacientams hemostazė buvo pasiekta per 7 ir 37 minutes.

<sup>b</sup>Remiantis bendru imties dydžiu 59: 1 pacientas nebuvo įtrauktas, nes jis dėl plaučių edemos buvo prijungtas prie ventiliacinės sistemos ir negalėjo ambuluoti ilgiau nei savaitę.

<sup>c</sup>Apibrėžta kaip kraujagyslių komplikacija, reikalaujanti kraujo perpylimo arba chirurginio gydymo, arba vietinė infekcija, kurią reikia gydyti antibiotikais, hospitalizuoti arba pailginti hospitalizacijos laiką, arba pašalinti pažeistas ląsteles

1-oje tyrimo dalyje sunkių kraujagyslių komplikacijų nepastebėta. 2-oje tyrimo dalyje nustatyta 1 sunki kraujagyslių komplikacija: pseudoaneurizma, apie kurią pranešta praėjus vienai dienai po procedūros. Įvykis reikalavo ultragarsu valdomo suspaudimo ir trombino injekcijos į pseudoaneurizmą ir prailgino paciento hospitalizaciją.

Iš penkių nepageidaujamų reiškinių, apie kuriuos pranešta 1-oje tyrimo dalyje, buvo 1 galimai su įtaisais susijęs nepageidaujamas reiškinys: nesunkus stipraus kraujavimo atvejis 1-ąją dieną po procedūros. Iš 19 nepageidaujamų reiškinių, apie kuriuos pranešta tyrimo 2 dalyje, buvo pastebėti trys nesunkūs su įtaisais susiję hematomos atvejai ir šeši galimai su įtaisais susiję nesunkūs reiškiniai, įskaitant tris nuolatinio difuzinio kraujavimo atvejus, dvi hematomas ir vienos kojos skausmą po fizinio krūvio.

2 dalyje 3 pacientai buvo laikomi, kuriems nepavyko gydymas: 2 dėl nepasiektos hemostazės nenaudojant kompresijos ir 1 dėl didelės kraujagyslių komplikacijos (pseudoaneurizmos).

1-oje tyrimo dalyje nebuvo gydymo sutrikimų.

Iš šešių 2-oje tyrimo dalyje aprašytų įtaiso gedimų trys netrukdė procedūrai, vienas buvo priskirtas naudotojo klaidai, vienas buvo įleidiklio nuotėkis, o kitas – pažeista užpildo jungtis. Pastarosios dvi problemos buvo išspręstos atlikus į C11202 įdiegtus modelio atnaujinimus.

2-oje klinikinio tyrimo prieš pateikiant rinkai dalyje nepranešama apie 6 mėnesių stebėjimo rezultatus dėl pacientų neatitikimo. Klinikinio tyrimo prieš pateikiant į rinką (EU-SE-001) 30 dienų rezultatai, atitinkantys klinikinėje literatūroje nurodytą stebėjimo laikotarpį, rodo, kad priemonė FemoSeal™ VCS yra saugi ir veiksminga.

### 1.4.2 Klinikinių tyrimų po pateikimo rinkai duomenų santrauka

Buvo atlikti 4 baigtiniai klinikiniai tyrimai po pateikimo į rinką, aprašyti toliau pateiktoje

**1.6 lentelėje.** Šie klinikiniai tyrimai nėra skelbiami ar prieinami internete.

**1.6 lentelė. Po pateikimo į rinką atlikti klinikiniai tyrimai**

| Po pateikimo į rinką atlikti klinikiniai tyrimai                                            |              |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                       |
|---------------------------------------------------------------------------------------------|--------------|--------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|
| Tyrimo pavadinimas                                                                          | Metai / CI   | Tyrimo tipas                                                       | Tikslai                                                                                                                                                                                                                                                                                                                                                                                                                                                | Etapai                                                                                                                                                                                                                                                                                                                                            | Galimi priėmimo kriterijai                                                                                            |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI | Tyrimas po pateikimo rinkai, naujos pakuotės priimtinas naudotojui | Po pateikimo rinkai, funkcionalumui registruoti buvo atliktas „FemoSeal Vascular® Closure System“ Nr. 11202 modelio, turinčio modifikuotą tiekimo sistemą, lyginant su pirmuoju modeliu Nr. 11200, rinkos tyrimas.<br><br>Tyrimo tikslas – gauti grįžtamąjį ryšį apie atnaujintas naudojimo instrukcijas (IFU), gydytojų ir slaugytojų mokymo projektą, patvirtinti rizikos analizės vertinimus ir prisidėti prie bet kokių produktų kokybės gerinimo. | 100 pacientų <ul style="list-style-type: none"> <li>63 vyrai / 37 moterys</li> <li>Vidutinis moterų amžius – 68 metai, vidutinis vyrų amžius – 65 metai</li> </ul> 2 Švedijos ligoninės, 6 gydytojai<br><br>112 įtaisų<br><br>Paciento įrašų formose (CRF) užfiksuoti duomenys<br><br>Planuojamas stebėjimo laikas – 30 minučių nuo taikymo laiko | Rezultatai<br><br>1. Naudojimo instrukcijos laikomos informatyviomis ir tinkamomis<br><br>2. Skubi hemostazė (91/100) |

|                                                                                   |                                                               |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                            |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
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| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008) | Dr. Nicolas Moes, Innsbruko medicinos universitetas, Austrija | Patvirtinimas po pateikimo rinkai | Šio tyrimo tikslas buvo įvertinti „FemoSeal®“, naudojamo įprastos klinikinės rutinos metu pacientams, kuriems atliekamas diagnostinis širdies kateterizavimas arba perkutaninė širdies intervencinė procedūra su 7F mova, saugumą ir veiksmingumą. | 50 pacientų iš eilės<br><br>Indikacija – diagnostinis arba invazinis širdies kateterizavimas iš bendrosios šlaunies arterijos<br><br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.6±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                                                                                                                                                          | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.6±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Pirminiai vertinimo kriterijai <ul style="list-style-type: none"><li>Pirminė veiksmingumo vertinamoji baigtis – LIH (laikas iki hemostazės) su difuziniu kraujavimu arba be jo, bet be jokios papildomos kompresijos, rankinės arba mechaninės.</li><li>Saugumo vertinamoji baigtis – nepageidaujamų reiškinių dažnis – nedidelės ir didelės kraujagyslių komplikacijos ir visi kiti nepageidaujami reiškiniai – sunkūs ir nesunkūs tyrimo metu (t. y. iki paciento išrašymo).</li></ul><br>Rezultatai <ul style="list-style-type: none"><li>Vidutinis laikas iki hemostazės</li><li>Diagnostika – 56,6 ± 29 sek.</li><li>Intervencinis 59,9 ± 16,2 sek.</li><li>Visi pacientai 57,8 ± 26,3</li><li>Visi pacientai be jokių problemų gali būti ambuluojami po 4 valandų poilsio lovoje.</li></ul><br>Saugos rezultatai <ul style="list-style-type: none"><li>49/50 (98 %) be kraujagyslių komplikacijų iki išrašymo iš ligoninės</li><li>Vidutinis išrašymo laikas 2,6 dienos</li><li>1/50 (2 %) nedidelis kraujavimas kitą dieną po nereikšmingos angiografijos</li></ul> |
| n                                                                                 | 50                                                            |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                            |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| men                                                                               | 35 (70%)                                                      |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                            |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| women                                                                             | 15 (30%)                                                      |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                            |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| PCI cases                                                                         | 15                                                            |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                            |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| age (yrs)                                                                         | 62.6±11.1                                                     |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                            |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| body mass index (kg/m²)                                                           | 25.4±6.7                                                      |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                            |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| systolic BP (mmHg)                                                                | 131.2±20.9                                                    |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                            |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| diastolic BP (mmHg)                                                               | 77.9±10.6                                                     |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                            |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| diabetes mellitus                                                                 | 9 (18%)                                                       |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                            |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| arterial hypertension                                                             | 34 (68%)                                                      |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                            |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| previous coronary intervention                                                    | 13 (26%)                                                      |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                            |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| preprocedure aspirin                                                              | 50 (100%)                                                     |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                            |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| preprocedure clopidogrel                                                          | 50 (100%)                                                     |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                            |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Procedural unfractionated heparin                                                 | 15 (30%)                                                      |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                            |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Procedural abciximab                                                              | 2 (4%)                                                        |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                            |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)    | 2009 RADI                                                     | Tyrimas po pateikimo rinkai       | Tyrimas turėtų informuoti, ar klientai / naudotojai pastebėjo kokių nors problemų dėl naujos pakuotės, ypač nesterilios išorinės „Tuvek“ / PET-PE maišelio pusės.<br><br>Tyrimas taip pat turėtų būti pateikta informacija apie tai,               | 25 įtaisai<br>4 Švedijos ligoninės<br><br>16/25 (64 %) pacientų buvo PCI pacientai, vartojantys stiprius antikoaguliantus                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Rezultatai<br>1. Su pakuote susijusios problemos – sėkmingai naudotos 21/25 (84 %); nesėkmingos buvo 4/25 (16 %) (1 – išbandytas naujas įleidiklis, 1 vidinis diskas perėjo per arteriotomiją, kai atliekant arteriotomiją pagrindiniame etape buvo pakeltas mygtukas ir i |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |

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|                                                                                                                                        |                                           |                                                                             | <p>ar gydantis gydytojas suvokia bet kokius prietaiso taikymo / įvedimo etapų skirtumus, palyginti su anksčiau naudotais įtaisais.</p> <p>Tyrimė taip pat turėtų būti atsižvelgta į tolesnius produktų kokybės gerinimo poreikius.</p>          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <p>pjūvio audinių kanalą ikištas išorinis diskas, 2 neatidėliotinos hemostazės nebuvo pasiektos nepaisant to, kad nebuvo jokių įvedimo problemų).</p> <p>2. Neatidėliotina hemostazė 19/25 (76 %) pacientams</p> <p>3. Kraujavimas 11/25 (44 %) – 9/25 (36 %), difuzinis kraujavimas / kraujavimas, 2/25 (8 %) hematomos</p> <p>Bendras įvykių koeficientas 19 %</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| <p>The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022)</p> | <p>2022 m./Terumo Medical Corporation</p> | <p>Prospektyvus, daugiacentrinis, stebėjimo tyrimas po pateikimo rinkai</p> | <p>Šio tyrimo tikslas – toliau įrodyti „FemoSeal™ VCS“ saugumą ir veiksmingumą, pasiekiant bendrosios šlaunies arterijos (BŠA) prieigos vietų hemostazę realiose tiriamuosiuose, kuriems atliekamos perkutaninės endovaskulinės procedūros.</p> | <ul style="list-style-type: none"> <li>Paciento stebėjimas po 30 dienų (<math>\pm 7</math> dienų) apsilankius ligoninėje arba paskambinus telefonu.</li> <li>Registracija: nuo 2021 m. gruodžio mėn. iki 2022 m. liepos mėn.</li> <li>Planuojama įtraukti 230 tiriamųjų, kuriems atliekamos diagnostinės arba intervencinės endovaskulinės procedūros, naudojant FemoSeal™.</li> </ul> <p>3 Europos vietos: Prancūzija (92 pacientai), Vokietija (38 pacientai), Belgija (100 pacientų).</p> | <ul style="list-style-type: none"> <li><b>Demografiniai duomenys / gretutinės ligos:</b> <ul style="list-style-type: none"> <li>- Lytis: 161 vyras (70 %) / 69 moterys 69 (30 %).</li> <li>- Vidutinis amžius: <math>70 \pm 12</math>.</li> <li>- KMI: <math>26,1 \pm 4,95</math> kg/m<sup>2</sup>.</li> <li>- Hipertenzija: 160 pacientų (69,6 %).</li> <li>- Dislipidemija: 128 (55,7 %).</li> <li>- Vainikinių arterijų liga: 42 (18,3%).</li> <li>- Dabartinis rūkantysis: 86 (37,6 %).</li> <li>- Buvęs rūkantysis: 66 (28,8 %).</li> <li>- Koronarinė širdies liga: 34 (14 %).</li> <li>- Ankstesnis miokardo infarktas: 18 (7,8 %).</li> <li>- Periferinės arterijos revaskuliarizacija: 12 (5,2 %) girnelės ir 83 (37,5 %) ir apatinės galūnės arterijos.</li> <li>- Antitrombotinis gydymas (bazinis): 211 (91,7 %), įskaitant 21 (9,1 %) dvigubą antitrombotinį gydymą (DAPT).</li> <li>- Burnos antikoaguliacija: 40 (17,4 %) pacientų.</li> </ul> </li> <li><b>Intervencijos ypatybės:</b> <ul style="list-style-type: none"> <li>- Nustatymas: ambulatorinė klinika 162</li> </ul> </li> </ul> |

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|  |  |  |  |  | <p>atvejai (70,4 %),<br/>ambulatorinė klinika 68 atvejai (29,6 %).</p> <p>- Vyraujanti indikacija: šlubavimas 147 atvejai (63,9 %).</p> <p>- Procedūra: 35 antegradiniai (15,3 %), 194 retrogradiniai (84,7 %).</p> <p>• <b>Pirminiai vertinimo kriterijai:</b></p> <p>- Saugumo (prieigos vietos galūnės nebuvimas sunkių komplikacijų per 6 valandas po procedūros) ir veiksmingumo (sėkminga hemostazė punkcijos vietoje) vertinamoji baigtis pasiekta 215/226 (95,1 %) [95 % PI: 91,46; 97,55] pacientams iš viso analizės rinkinio ir 215/230 (93,5 %) [95 % PI 89,47, 96,30] pacientams iš "FemoSeal™" gydomo rinkinio.</p> <p>- Veiksmingumo vertinamoji baigtis buvo pasiekta 219/226 (96,9 %) pacientų PI [93,7, 98,7].</p> <p>- Saugumo vertinamoji baigtis pasiekta 220/230 (95,2 %) [95 % PI: 92,15, 97,90] pacientų.</p> <p>• <b>Antriniai vertinimo kriterijai:</b></p> <p>- Nesant nedidelių prieigos vietos komplikacijų šešias valandas po procedūros, pasiekta 225/230 (97,8 %) [95 % PI: 95,00; 99,29].</p> <p>- 219/230 (95,2 %) [95 % PI: 91,60; 97,59] pacientų po procedūros praėjus šešioms valandoms iki 30 dienų nebuvo didelių ir</p> |
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|  |  |  |  |  | <p>nedidelių prieigos vietos komplikacijų.</p> <p>- Vidutinis laikas iki hemostazės naudojant FemoSeal™ VCD: 0,42 (0,25; 0,50) minutės.</p> <p>- Vidutinis laikas ambuliacijai: 5,00 (4,54; 5,50) minutės.</p> <p>- Vidutinė buvimo ligoninėje trukmė: 23,98 (22,72, 25,00) valandos.</p> <p>- FemoSeal™ VCS tinkamumas naudoti: „lengva“ arba „labai lengva“ įvesti 98,7 % atvejų (21 (9,2 %) „lengva“ įvesti, 205 (89,5 %) „labai lengva“ įvesti), 226 (98,3 %) atvejų įvesti pasipriešinimo nėra arba jis yra mažas.</p> <p>152/230 (66,1 %) pacientų, gydomų naudojant kreipiamąją vielą, pateiktą FemoSeal™ rinkinyje (0,038 colio GW) ir rekomenduojamą FemoSeal™ rinkinyje, neturėjo jokių praneštų prietaiso trūkumų ar nepageidaujamų reiškinių.</p> |
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2006 m. atliktas tyrimas siekiant patvirtinti dabartinio įtaiso saugumą ir efektyvumą naudojant patobulintą įvedimo sistemą ir gauti grįžtamąjį ryšį apie FemoSeal™ VCS naudojimo instrukcijas ir mokymų programą. Tyrime dalyvavo 100 pacientų, o pirminė vertinamoji baigtis – ar buvo pasiekta hemostazė, ar reikėjo papildomo rankinio ar mechaninio suspaudimo. Šiame tyrime padaryta išvada, kad daugeliu atvejų FemoSeal™ VCS naudojimas buvo sėkmingas (91 % pasiekė neatidėliotiną hemostazę).

2008 m. tyrime dalyvavo 50 pacientų, kurie vertino FemoSeal™ VCS saugumą ir veiksmingumą, kai ji buvo naudojama įprastos klinikinės procedūros metu pacientams, kuriems atliekamas širdies kateterizavimas su 7Fr mova. Pagrindinis tyrimo tikslas buvo surinkti duomenis apie laiką iki hemostazės ir laiką iki ambuliacijos be papildomo suspaudimo – rankinio ar mechaninio. Tyrimo rezultatai parodė, kad vidutinis laikas iki hemostazės buvo 57,8 sekundės, o visi pacientai ambuliavo po 4 valandų poilsio lovoje.

2009 m. atliktas tyrimas buvo skirtas įvertinti naują FemoSeal™ VCS pakuotę. Tyrime dalyvavo 25 pacientai. Pirminė vertinamoji baigtis – ar vartotojas susidūrė su problemomis dėl pakuotės. Vartotojai nepastebėjo jokių problemų dėl naujos FemoSeal™ VCS pakuotės. Šis tyrimas taip pat surinko duomenis apie laiką iki hemostazės.

Šio 2022 tyrimo tikslas – toliau įrodyti FemoSeal™ VCS saugumą ir veiksmingumą, pasiekiant bendrosios šlaunies arterijos (BŠA) prieigos vietų hemostazę realiose tiriamuosiuose, kuriems atliekamos perkutaninės endovaskulinės procedūros. Tyrime dalyvavo 230 pacientai. Pirminiai registro tikslai yra procedūrinė sėkmė (t. y. sėkminga punkcijos vietos hemostazė) ir sunkių komplikacijų (pvz., kraujagyslių pažeidimo, prieigos vietos kraujavimo, prieigos vietos infekcijos, pakartotinio rankinio suspaudimo ir naujos prieigos vietos ipsilateralinės ūminės kojos išemijos) sumažėjimas. Tyrimas parodė, kad FemoSeal™ VCS veiksmingai veikia realioje aplinkoje ir užtikrina veiksmingą hemostazę bei mažą prieigos vietos komplikacijų dažnį pacientams, kuriems atliekamos periferinės endovaskulinės intervencijos. Jis pasižymi geromis eksploatacinėmis savybėmis, trumpu hemostazės laiku ir, pagal atsiliepimus, yra patogus naudoti operatoriui, todėl FemoSeal™ VCS yra vertingas šlaunies prieigos uždarymo įtaisas.

### 1.4.3 Klinikinio stebėjimo po pateikimo rinkai duomenų santrauka

#### 1.4.3.1 Po pateikimo į rinką atlikti klinikiniai tyrimai

Atliktų klinikinių stebėjimų po pateikimo rinkai santrauka pateikiama toliau esančioje 1.7 lentelėje.

**1.7 lentelė Tolesnė klinikinio stebėjimo veikla po pateikimo rinkai**

| Užbaigta klinikinio stebėjimo veikla po pateikimo rinkai                  |            |                                                                   |                                                                                                                                                                            |                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                   |
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| Veiklos pavadinimas                                                       | Metai / CI | Tyrimo tipas                                                      | Tikslai                                                                                                                                                                    | Etapai                                                                                                                                                   | Galimi priėmimo kriterijai                                                                                                                                                                                                                                                                                                                                                                                        |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021 TMC   | Klinikinis tyrimas po pateikimo rinkai - aukštos kokybės apklausa | Tyrimas po pateikimo į rinką, skirtas rinkti prospektyvinius atsiliepimus, susijusius su Europos Sąjungos rinkoje platinamo „FemoSeal™ Vascular Closure Device“ naudojimu. | <ul style="list-style-type: none"> <li>120 atvejai</li> <li>8 unikalūs gydytojai, turintys &gt; 5 metų patirtį</li> <li>Keletas Europos šalių</li> </ul> | <b>1-5 Mastelio prietaiso vertinimai. Tyrimo ataskaitos</b> <ul style="list-style-type: none"> <li>Patvirtinimo kriterijai <ul style="list-style-type: none"> <li>3-5 reitingai laikomi palankiais</li> <li>Visuose teiginiuose turi būti ≥ 80 % teigiamų atsiliepimų</li> </ul> </li> <li>Rezultatai <ul style="list-style-type: none"> <li>Negautas nei vienas tyrimo teiginys &gt; 20 %</li> </ul> </li> </ul> |

| Užbaigta klinikinio stebėjimo veikla po pateikimo rinkai            |                  |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
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|                                                                     |                  |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                            | nepalankių atsakymų <ul style="list-style-type: none"> <li>○ Nebuvo užpildyta jokių skundų dėl gaminio</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                        |
| 20210298 – 0.035” and 0038” Guidewire Clinical Survey Report (2021) | 2021 TMC         | Klinikinis tyrimas po pateikimo rinkai - aukštos kokybės apklausa | Tyrimas po pateikimo rinkai, siekiant surinkti prospektyvinius atsiliepimus, susijusius su 0,035 col. kreipiamosios vielos, pateikiamos kartu su 6 prancūziškojo dydžio „Angio-Seal™“ VIP kraujagyslių uždarymo įtaisu (VCD), ir 0,038 col. kreipiamosios vielos, pateikiamos kartu su 8 prancūziškojo dydžio „Angio-Seal™“ VIP VCD ir FemoSeal kraujagyslių uždarymo sistema, platinama Europos Sąjungos rinkose, naudojimu. | <ul style="list-style-type: none"> <li>• 0,035 col. kreipiamosios vielos tyrimai <ul style="list-style-type: none"> <li>○ 106 tyrimai</li> <li>○ 64 gydytojai</li> </ul> </li> <li>• 0,038 col. vielos tyrimai <ul style="list-style-type: none"> <li>○ 109 tyrimai</li> <li>○ 55 gydytojai</li> </ul> </li> <li>• 12 retrospektyviniai tyrimai</li> </ul> | <b>1-5 Mastelio prietaiso vertinimai. Tyrimo ataskaitos</b> <ul style="list-style-type: none"> <li>• Patvirtinimo kriterijai <ul style="list-style-type: none"> <li>○ 3-5 reitingai laikomi palankiais</li> <li>○ Visuose teiginiuose turi būti <math>\geq 80\%</math> teigiamų atsiliepimų</li> </ul> </li> <li>• Rezultatai <ul style="list-style-type: none"> <li>○ Visos kreipiamosios vielos gavo priimtinus įvertinimus</li> <li>○ Nebuvo pateikta jokių skundų dėl gaminio</li> </ul> </li> </ul> |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey              | 2023-2024 TMC/TE | Klinikinis tyrimas po pateikimo rinkai - aukštos                  | Rinkti prospektyvinius atsiliepimus, susijusius su FemoSeal VCS naudojimu kartu su ES rinkoje                                                                                                                                                                                                                                                                                                                                 | <ul style="list-style-type: none"> <li>• 126 tyrimai</li> <li>• 7 tyrimų centrai</li> <li>• 5 šalys</li> <li>• 2023 m. lapkričio 14 d.- 2024 m. birželio 11 d.</li> </ul>                                                                                                                                                                                  | <b>5 Mastelio prietaiso vertinimai. Tyrimo ataskaitos</b> <ul style="list-style-type: none"> <li>• Patvirtinimo kriterijai <ul style="list-style-type: none"> <li>○ 3-5 reitingai laikomi palankiais</li> </ul> </li> </ul>                                                                                                                                                                                                                                                                              |

| Užbaigta klinikinio stebėjimo veikla po pateikimo rinkai                                        |  |                     |                                              |                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-------------------------------------------------------------------------------------------------|--|---------------------|----------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Report:<br>Addressing<br>Gaps<br>Identified in<br>CER-FS-<br>2021 and<br>CER-FS-<br>2022 (2023) |  | kokybės<br>apklausa | platinamomis<br>kreipiamosiomis<br>vielomis. | <ul style="list-style-type: none"> <li>Gydytojo specialybė: <ul style="list-style-type: none"> <li>Kraujagyslių chirurgija</li> <li>Intervencinė radiologija</li> <li>Angiologija</li> </ul> </li> </ul> | <ul style="list-style-type: none"> <li>Visuose teiginiuose turi būti <math>\geq 80\%</math> teigiamų atsiliepimų</li> <li>Jei šiame tyrime pasitaiko nepageidaujamų reiškinių, jie turi būti tokie, kokių tikimasi pagal rizikos valdymo duomenis.</li> <li>Pacientų demografiniai duomenys <ul style="list-style-type: none"> <li>Moterys: 29,4 % (37/126)</li> <li>Vyrai: 69,8 % (88/126)</li> <li>Lytis neatskleista: 0,8 (1/126)</li> <li>Amžius &gt;75 metai: 31,7 %</li> </ul> </li> <li>Rezultatai <ul style="list-style-type: none"> <li>Kreipiamoji viela, pateikiama su FemoSeal™ VCS: 101/126 (80,2 %).</li> <li>Procedūros trukmė (minutės): 63,4 (36,6) (vidurkis (standartinis nuokrypis)); 57,0 (36,0-81,0) (mediana (tarpkvartilinis režis))</li> <li>Visi FemoSeal™ VCS eksploatacinių savybių įvertinimai buvo teigiami.</li> </ul> </li> </ul> |

| Užbaigta klinikinio stebėjimo veikla po pateikimo rinkai |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                         |
|----------------------------------------------------------|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                          |  |  |  |  | <ul style="list-style-type: none"> <li>○ Visų FemoSeal™ VCS tiekiamų kreipiamųjų vielų įvertinimai buvo teigiami.</li> <li>○ Vienas (0,8 %) nepageidaujamas reiškinys: FemoSeal™ VCS diskai galėjo būti netinkamai sulygiuoti, nes buvo naudojama standi kreipiamoji viela (Boston Scientific Amplatzer Super Stiff, 75 cm, 0,035 colio), kurią reikia suspausti rankiniu būdu, kad būtų pasiekta hemostazė.</li> </ul> |

Terumo Medical Corporation atliko tris aukštos kokybės tyrimus apklausiant priemonę naudojančius gydytojus dabartiniu ataskaitiniu laikotarpiu (2019 m. rugsėjo 1 d. - 2024 m. rugpjūčio 31 d.).

FemoSeal™ klinikinių tyrimų metu buvo renkami aktyvūs klinikiniai duomenys, susiję su FemoSeal™ VCS saugumu ir veiksmingumu klinikinio naudojimo metu. Apklausoje buvo nagrinėjami klausimai apie bendrą prietaisą ir susijusius priedus, įskaitant 0,038 col. kreipiamąją vielą, ir jų tiesioginę sąveiką. Klinikinių kreipiamosios vielos tyrimų metu surinkti aktyvūs klinikiniai duomenys apie saugumą ir veiksmingumą klinikinio 0,038 col. kreipiamosios vielos, tiekiamos su FemoSeal™ VCS, naudojimo metu. Apklausoje metu buvo nagrinėjami klausimai, susiję su bendru kreipiamosios vielos naudojimu, pradedant nuo įvedimo per procedūrinę movą į kraujagyslę iki vielos pašalinimo.

FemoSeal™ VCS ir 0,038 col. kreipiamoji viela, teikiama su įtaisu, gavo visus priimtinius įvertinimus ir šešis (6) nusiskundimus dėl įtaiso bei devynis (9) pranešimus dėl kreipiamosios vielos, pagrįstus aukštos kokybės klinikinių tyrimų pastabų įvertinimu. Skundai buvo įvertinti FemoSeal™ ir kreipiamosios vielos atžvilgiu ir buvo įvertinti kaip Terumo tyrimo po pateikimo rinkai proceso dalis. Naujos rizikos ar rizikos lygių nenustatyta.

Gydytojų naudotojų apklausa buvo atlikta 2024 m. kaip PMCF veiklos dalis. Tyrimo rezultatai parodė, kad FemoSeal™ VCS eksploatacinės savybės ir bendra sauga buvo vertinami labai teigiamai. Buvo įrodytas ir kitų nei standartinių, pateiktų su FemoSeal™ VCS, kreipiamųjų vielų suderinamumas.

#### **1.4.3.2 Nuolatinis arba planuojamas klinikinis stebėjimas po pateikimo rinkai**

TMC turi du vykdomus/ planuojamus klinikinius stebėjimus po pateikimo rinkai. Be to, bus atlikta klinikinė apklausa, kurios metu bus galima gauti grįžtamąjį ryšį, susijusį su ES rinkoje platinamos FemoSeal™ VCS kreipiamosios vielos naudojimu. Apklausą pildys gydytojai, kad būtų galima iširti, kokias kreipiamąsias vielas jie naudojo procedūros metu. Šio tyrimo tikslas - spręsti nustatytą trūkumą, t. y. literatūros ir išorinių ekspertų komentarų apie FemoSeal™ VCS suderinamumą su ne Terumo prekės ženklo kreipiamosiomis vielomis, stoką. Atsiliepimai apima techninius rezultatus, kliniskines charakteristikas ir saugą, susijusius su įtaiso veikimu su skirtingomis kreipiamosiomis vielomis.

#### **1.4.4 Sisteminės literatūros peržiūros duomenų santrauka**

Terumo Medical Corporation atlieka sisteminės literatūros apžvalgas, kad surinktų ir įvertintų klinikinio saugumo ir veiksmingumo duomenis iš paskelbtų tyrimų, susijusių su FemoSeal™ VCS ir (arba) panašių įtaisų. Publikuotos literatūros metinės patikros tikslas - nustatyti anksčiau nežinomus šalutinius poveikius, stebėti žinomus šalutinius poveikius, nustatyti kylančią riziką ir nustatyti galimą sistemingą netinkamą FemoSeal™ VCS naudojimą ar naudojimą ne pagal nurodymus.

Naujausioje sistemingoje literatūros apžvalgoje, kuri apėmė laikotarpį nuo 2019 m. rugsėjo 1 d. iki 2024 m. rugpjūčio 31 d., buvo pateikti 29 paskelbti tyrimai, kuriuose buvo pateikti klinikinio saugumo ir veiksmingumo duomenys apie FemoSeal™ VCS. Dvidešimt trijuose šaltiniuose buvo minimas FemoSeal™ VCS naudojimas pagal paskirtį, o devyniuose tyrimuose buvo minimas naudojimas ne pagal paskirtį. Apskritai literatūros apžvalga apie FemoSeal™ VCS naudojimo tyrimus rodo tiriamą populiaciją, kuri yra tipiška ES pacientams, kuriems atliekamos perkutaninio kraujagyslių kateterizavimo procedūros. Šių 23 recenzuojamų publikacijų, kuriose minimas naudojimas pagal paskirtį, sąrašą žr. **3 skyriuje**.

Klinikinis veiksmingumas buvo įvertintas šiomis priemonėmis:

- Laikas iki hemostazės yra geresnis arba panašus į šiuo metu taikomą poodinio bendrojo šlaunies arterijos uždarymo standartą.

- Laikas iki ambuliacijos yra geresnis už ar panašus į šiuo metu taikomą perkutaninio bendrojo šlaunies arterijos uždarymo standartą.
- Pooperacinių komplikacijų dažnis yra panašus arba mažesnis už dabartinius priežiūros standartus

Remiantis šiomis klinikinėmis veiksmingumo priemonėmis, literatūros apžvalgoje pateikti duomenys parodė, kad FemoSeal™ VCS galima sėkmingai naudoti uždariant šlaunies arterinę punkciją (arteriotomiją) pacientams, kuriems buvo atliktas perkutaninis kateterizavimas naudojant 7Fr ar mažesnę procedūrinę movą. Visiška hemostazė buvo pasiekta daugumai pacientų (79,65-100 %) ir buvo siejama su vidutiniu hemostazės pasiekimo laiku – 0,5 min. bei vidutiniu paciento išrašymo laiku – 3 dienomis. 69,2-86,7 % pacientų galėjo vaikščioti praėjus 5 val. po operacijos, vidutinė pooperacinio lovos režimo trukmė buvo 349 min. FemoSeal™ VCS nesėkmės buvo stebėtos 3,68-4 % atvejų, o papildomo rankinio suspaudimo prireikė 0,9-4,4 % procedūrų.

Klinikinis saugumas buvo įvertintas pagal nepageidaujamus reiškinius, įskaitant, bet neapsiribojant:

- Kraujavimu
- Hematoma
- Pseudoaneurizma
- Kraujosruva
- Arterioveninė fistulė
- Infekcija
- Mirtis

Kiekvienam iš šių nepageidaujamų reiškinių FemoSeal™VCS pasireiškimo dažnis įtrauktuose tyrimuose buvo mažesnis arba panašus į pranešamus dažnius, naudojant rankinį suspaudimą ir kitus kraujagyslių uždarymo įtaisus.

Peržiūrint 10 ligos ataskaitas nenustatyta jokių nepageidaujamų reiškinių, nes nebuvo nustatyta jokios naujos, nenumatytos, atsirandančios ar nepriimtinos rizikos.

Bendras FemoSeal™ VCS naudojimo efektyvumas diagnostinės angiografijos ar intervencinių procedūrų metu priklauso nuo daugelio veiksnių, tokių kaip: lytis, amžius, paciento anatomija, gretutinės ligos, punkcijos vietos anatomicinė padėtis, gydytojo patirtis, kraujagyslių uždarymo įrenginio įvedimo metodas, pooperacinė priežiūra ir kt. Be techninės sėkmės, įskaitant hemostazės pasiekimą, FemoSeal™ VCS taip pat suteikė klinikinę naudą, susijusią su šlaunies arterijos punkcijos vietos uždarymu, taip sutrumpėjo hemostazės pasiekimo laikas ir laikas iki ambuliacijos. FemoSeal™ VCS eksploatacinių savybių rezultatai atitinka tikėtinus šio tipo priemonių rezultatus, kai jos naudojami pagal paskirtį. Kai kuriuose šiuo paieškos laikotarpiu rastuose šaltiniuose

priemonė buvo naudojama ne bendrojoje šlaunies arterijoje, o kitoje anatomicinėje vietoje, taip pat arteriotomijoms, didesnėms nei 7 prancūziškasis dydis, uždaryti – tai laikoma naudojimu ne pagal paskirtį.

Atlikus peržiūrą nebuvo nustatyta jokių nežinomų šalutinių poveikių, atsirandančių rizikų ar galimo sisteminio netinkamo priemonės naudojimo. Tačiau, jei FemoSeal™ VCS atsargiai naudoja išmokyti gydytojai, medicinos priemonė veikia kaip naudinga ir būtina klinikinė priemonė. Bendrais bruožais, tikslinė terapija ir tuo pačiu FemoSeal™ VCS atitinka šiuo metu esantį klinikinį poreikį, susijusį su kraujagyslių prieigos komplikacijų gydymu.

Apskritai šioje literatūros apžvalgoje pateiktais duomenimis nenustatyta jokių anksčiau nežinomų klinikinės aplinkos veiksmingumo ar saugos problemų arba nepageidaujamo poveikio, kuris pasireiškė didesne nei tikėtasi / priimtina apimtimi. Todėl iš šios literatūros apžvalgos galima daryti išvadą, kad priemonė FemoSeal™ VCS, naudojama suspaudimui siekiant pasiekti hemostazę arteriotomijos metu po perkutaninio kateterizavimo, ir toliau veikia taip, kaip tikėtasi, ir nėra susijusi su rimtais saugos įvykiais.

#### 1.4.5 Stebėsenos po pateikimo rinkai duomenų santrauka

Įdiegta aktyvi PMS sistema ir kas mėnesį atliekama visų skundų peržiūra, laikantis vidaus gamybos procedūrų. Skundų duomenys buvo analizuojami laikotarpiu nuo 2019 m. rugsėjo 1 d. iki 2024 m. rugpjūčio 31 d. Iš viso gamintojui buvo pateiktos 28 medicinos priemonių budrumo (MPB) ataskaitos ir 476 klientų skundai. Iš 28 MPB ataskaitų 27 buvo susijusios su nepageidaujamais reiškiniais, o viena su priemonės gedimu. Per ataskaitinį laikotarpį mirė du žmonės, tačiau nė vienas iš praneštų mirčių nebuvo laikomas susijusiu su tiriamąja priemone. Iš 476 gamintojui pateiktų skundų dažniausia skundų priežastis buvo įvedimo sunkumai (146 atvejai, 0,0142 % atvejų dažnis). Ištraukimo sunkumai buvo antras dažniausiai pasitaikantis įvykis, kurio dažnis yra 0,0126 % (130 įvykių).

FemoSeal Vascular Closure System visame pasaulyje parduodama daugiau nei 1 030 136 vienetų, o Europos ekonominėje erdvėje - 827 843 vienetai. Pasauliniais pardavimais grindžiamas apskaičiuotas skundų dažnis yra 0,046 %. Bendras klientų skundų lygis yra labai mažas. Nebuvo nustatyta jokių naujų pavojų, kurie nebūtų įtraukti į naudojimo instrukcijas ir rizikos dokumentus.

Nepageidaujamo šalutinio poveikio pasireiškimo dažnis nurodytas **1.2 lentelėje**. Skunduose nenustatyta jokių naujų nenumatytų, atsirandančių ar nepriimtinių rizikų. Žinomo nepageidaujamo šalutinio poveikio dažnis ir sunkumas reikšmingai nepadidėjo.

#### 1.4.6 Bendra klinikinio veiksmingumo ir saugos santrauka

FemoSeal™ VCS skirta naudoti uždariant bendrąją šlaunies arterijos punkciją (arteriotomiją) pacientams, kuriems buvo atliktas perkutaninis kateterizavimas naudojant 7F (2,33 mm) arba mažesnę procedūrinę movą. Šis klinikinis vertinimas pagrįstas išsamia turimų klinikinų



duomenų prieš pateikimą rinkai ir po pateikimo rinkai bei literatūros, susijusios su numatytuoju „FemoSeal™ VCS“ naudojimu, analize.

Atlikta išsami paskelbtos literatūros apžvalga, apimanti laikotarpį nuo 2019 m. rugsėjo 1 d. iki 2024 m. rugpjūčio 31 d. Įrodymų rinkinyje buvo 29 FemoSeal™ VCS tyrimai. Klinikinio vertinimo metu pateikti įrodymai leidžia daryti išvadą, kad tiriamasis prietaisas yra saugus ir veiksmingas, kai naudojamas kaip nurodyta, o bet kokia rizika ar nepageidaujamas šalutinis poveikis, kuris gali būti susijęs su prietaisu įprastomis naudojimo sąlygomis, yra priimtina rizika, palyginti su nauda pacientui. Tiriamųjų prietaisų veikimo rezultatai atitinka tikėtinus šio tipo prietaisų rezultatus, kai jie naudojami pagal paskirtį.

Galimi nepageidaujami šalutiniai poveikiai, susiję su FemoSeal™ VCS naudojimu, apima nepageidaujamus reiškinius, apie kuriuos paprastai pranešama naudojant alternatyvias arteriotomijos uždarymo priemones, pvz., kraujavimą ir hematomą. Apskritai nepageidaujamų reiškinių, apie kuriuos pranešta naudojant FemoSeal™ VCS, dažnis yra panašus į dažnį, nurodytą naudojant rankinį suspaudimą ir panašius kraujagyslių uždarymo prietaisus. Konkrečiai, kraujavimo ir hematomos dažnis naudojant FemoSeal™ VCS yra mažesnis nei nurodytas panašių kraujagyslių uždarymo prietaisų dažnis. Anksčiau buvo nustatyti visi šalutiniai reiškiniai, apie kuriuos pranešta tiek paskelbtoje literatūroje, tiek stebėjimo po pateikimo rinkai metu (žr. **1.3 skyrių**).

Turimi duomenys apie FemoSeal VCS klinikinę saugą ir veiksmingumą rodo, kad naudojant šį kraujagyslių uždarymo prietaisą paciento nauda yra didesnė už galimą riziką, kai jis naudojamas pagal naudojimo instrukciją.

Kaip nurodyta ankstesniuose skyriuose, FemoSeal™ VCS pateikti duomenys rodo duomenų, susijusių su vertinama priemone, (pvz., priemonės naudojimo, saugos rezultatų, klinikinio veiksmingumo ir klinikinės naudos), nustatytų lygiaverčių priemonių ir duomenų, susijusių su panašiomis priemonėmis, išvardytomis standartinėje praktikoje, nuoseklumą.

Atlikus saugos duomenų kryžminę analizę, nebuvo nustatyta jokių neatitikimų tarp:

- Duomenų, minimų naujausioje mokslo ir technikos srityje
- Vertinamam įrenginiui būdingų duomenų
- Rizikos valdymo faile (-uose) nurodytų duomenų
- Duomenys, nurodyti ženklinime ir (arba) naudojimo instrukcijoje (t. y. pašalinama liekamoji rizika, kuri turi būti perduota naudotojui).

Klinikinis saugumas įrodytas nedideliu komplikacijų dažniu, nustatytu paskelbtoje recenzuojamoje klinikinėje literatūroje, bendrovės remiamuose klinikiniuose tyrimuose, duomenų po pateikimo rinkai apžvalgoje, be pasitraukimo iš rinkos. Nenustatytos jokios problemos dėl veikimo, peržiūroje literatūroje aptiriamas FemoSeal™ VCS naudojimas, kuris atitiko gamintojo numatytąją paskirtį.

## 1.5 Galimos diagnostinės arba gydymo alternatyvos

Rankinis suspaudimas tradiciškai naudojamas hemostazei pasiekti arteriotomijos vietoje po kraujagyslių kateterizavimo. Rankinis suspaudimas buvo susijęs su paciento ilgalaikiu (iki 8 valandų po procedūros) imobilizavimu ir dideliu diskomfortu bei ilgesniu buvimu ligoninėje. Neseniai atliktoje sisteminėje apžvalgoje nustatyta, kad laiko hemostazei pasiekti naudojant rankinę kompresiją mediana buvo 20,8 minutės.<sup>1</sup>

Rankinio suspaudimo alternatyvos apima išorinius hemostatinius prietaisus, kurie mechanškai suspaudžia arteriotomijos vietą. Šie įtaisai nesutrumpina laiko iki hemostazės ar ambuliacijos, bet sumažina personalui keliamus reikalavimus, pakeisdami rankinį suspaudimą mechanine kompresija. Nepageidaujamų reiškinių dažnis, susijęs su mechaninės kompresijos naudojimu, yra panašus į dažnį su rankiniu suspaudimu.

Kraujagyslių uždarymo įtaisai, tokie kaip FemoSeal™ VCS, skirti arteriotomijai uždaryti. Jų tikslas – sutrumpinti laiką iki hemostazės ir sudaryti sąlygas ankstesnei ambuliacijai. Neseniai atlikta sisteminė apžvalga, apimanti 13 komercinių prietaisų, parodė, kad vidutinis laikas hemostazei pasiekti naudojant kraujagyslių uždarymo įtaisą buvo 5,4 minutės. Atskirų kraujagyslių uždarymo įtaisų laiko iki hemostazės mediana svyravo nuo 1 minutės (FemoSeal™ VCS) iki 14 minučių; tuo tarpu daugumos įtaisų buvo nuo 4 iki 10 minučių.<sup>1</sup>

Dažniausiai pranešama apie nepageidaujamus reiškinius, susijusius su arteriotomijos vietos uždarymu, naudojant rankines kompresijas, išorinius hemostatinius įtaisus arba kraujagyslių uždarymo įtaisus, yra hematoma, kraujavimas prieigos vietoje, pseudoaneurizma, arterioveninė fistulė ir infekcija. Ta pati sisteminė apžvalga (34 atsitiktinių imčių kontroliuojami tyrimai, 14 401 pacientas) nustatė, kad nepageidaujamų reiškinių dažnis tarp rankinio suspaudimo ir kraujagyslių uždarymo įtaisų naudojimo buvo panašus, išskyrus tai, kad kraujavimas buvo šiek tiek didesnis naudojant kraujagyslių uždarymo įtaisus.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Sisteminga atsitiktinių imčių kontroliuojamų tyrimų, kuriuose lyginamas rankinis suspaudimas su kraujagyslių uždarymo prietaisais diagnostinėms ir terapinėms arterijų procedūroms, apžvalga. Tarptautinė chirurgijos technologija, 27, 32–44.*

## 1.6 Siūlomas naudotojo profilis ir mokymai

Kraujagyslių uždarymo sistemos FemoSeal™ Vascular Closure System numatytieji naudotojai yra gydytojai, turintys kvalifikaciją atlikti arterinę prieigą ir uždarymą atliekant endovaskulines procedūras per bendrąją šlaunies arteriją ir dalyvavę Terumo Medical Corporation FemoSeal™ gydytojų mokymo programoje.

## 1.7 Atitinkami darnieji ir bendrieji standartai

| Nuoroda į standartą | Dabartiniai atitikties / peržiūros metai | Aprašas                                                                                                                                  |
|---------------------|------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070           | 2014/AMD1:2018                           | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| LT ISO 11070        | 2014/A1:2018                             | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA rekomendacijos  | 2021 m. gegužės 20 d.                    | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052          | 2015                                     | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213          | 2017                                     | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503          | 2020 m.                                  | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182          | 2019                                     | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |
| LT ISO 13485        | 2016/A11:2021                            | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 13485           | 2016                                     | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 14644-1         | 2015                                     | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                  |
| LT ISO 14644-1      | 2015                                     | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                  |

| Nuoroda į standartą   | Dabartiniai atitikties / peržiūros metai | Aprašas                                                                                                                                                                  |
|-----------------------|------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14644-2           | 2015                                     | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| LT ISO 14644-2        | 2015                                     | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3           | 2019                                     | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| LT ISO 14644-3        | 2019                                     | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1           | 2003                                     | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| LT ISO 14698-1        | 2003                                     | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2           | 2003/TC1:2004                            | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| LT ISO 14698-2        | 2003/TC 1:2004                           | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| USP <788>             | NETAIKOMA                                | PARTICULATE MATTER IN INJECTIONS                                                                                                                                         |
| ES farmakopėja 2.9.19 | NETAIKOMA                                | Particulate Contamination: Sub-Visible Particles                                                                                                                         |
| IEC 62366-1           | 2015                                     | Medical devices — Part 1: Application of usability engineering to medical devices                                                                                        |
| LT 62366-1            | 2015                                     | Medical devices — Part 1: Application of usability engineering to medical devices                                                                                        |

| Nuoroda į standartą | Dabartiniai atitikties / peržiūros metai | Aprašas                                                                                                              |
|---------------------|------------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| LT ISO 14971        | 2019/A11:2021                            | Medical devices — Application of risk management to Medical devices                                                  |
| ISO 14971           | 2019                                     | Medical devices — Application of risk management to Medical devices                                                  |
| ASTM F1980          | 2016                                     | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| LT ISO 10993-1      | 2020 m.                                  | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1         | 2018 m.                                  | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| LT ISO 10993-2      | 2006                                     | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2         | 2006                                     | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| LT ISO 10993-3      | 2014                                     | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3         | 2014                                     | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| LT ISO 10993-4      | 2017                                     | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4         | 2017                                     | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| LT ISO 10993-5      | 2009                                     | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| ISO 10993-5         | 2009                                     | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| LT ISO 10993-6      | 2016                                     | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |

| Nuoroda į standartą | Dabartiniai atitikties / peržiūros metai | Aprašas                                                                                                                                    |
|---------------------|------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-6         | 2016                                     | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| LT ISO 10993-10     | 2023                                     | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| ISO 10993-10        | 2021                                     | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| LT ISO 10993-11     | 2018 m.                                  | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| ISO 10993-11        | 2017                                     | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| LT ISO 10993-12     | 2021                                     | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| ISO 10993-12        | 2021                                     | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| LT ISO 10993-17     | 2009                                     | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17        | 2002                                     | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18        | 2020/A1:2022                             | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |
| LT ISO 10993-18     | 2020/A1:2022                             | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |
| LT ISO 10993-23     | 2021                                     | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |
| ISO 10993-23        | 2021                                     | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |

| Nuoroda į standartą | Dabartiniai atitikties / peržiūros metai | Aprašas                                                                                                                                                                      |
|---------------------|------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F2382          | 2018 m.                                  | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756           | 2017                                     | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>            | NETAIKOMA                                | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>           | NETAIKOMA                                | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72:2011 | 2019                                     | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| LT ISO 11135        | 2014/A1:2019                             | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135           | 2014/A1:2018                             | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| LT ISO 10993-7      | 2008/A1:2022                             | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |
| ISO 10993-7         | 2008/A1:2019                             | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                                            |
| LT 556-1            | 2024                                     | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices              |

| Nuoroda į standartą | Dabartiniai atitikties / peržiūros metai | Aprašas                                                                                                                                  |
|---------------------|------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| LT ISO 11737-1      | 2018/A1:2021                             | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products    |
| ISO 11737-1         | 2018/A1:2021                             | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products    |
| LT ISO 11138-1      | 2017                                     | Sterilization of health care products - Biological indicators - Part 1: General requirements                                             |
| ISO 11138-1         | 2017                                     | Sterilization of health care products - Biological indicators - Part 1: General requirements                                             |
| LT ISO 11138-2      | 2017                                     | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| ISO 11138-2         | 2017                                     | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| LT ISO 15223-1      | 2016                                     | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| ISO 15223-1         | 2016                                     | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| EN 1041             | 2008/A1:2013                             | Information supplied by the manufacturer of medical devices                                                                              |
| LT ISO 11607-1      | 2020/A1:2023                             | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| ISO 11607-1         | 2019/A1:2023                             | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |



| Nuoroda į standartą    | Dabartiniai atitikties / peržiūros metai | Aprašas                                                                                                                                                                    |
|------------------------|------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| LT ISO 11607-2         | 2020/A1:2023                             | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ISO 11607-2            | 2019/A1:2023                             | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169             | 2016                                     | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886 / F1886M-16 | 2016                                     | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825             | 2018 m.                                  | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096             | 2011 (R 2019)                            | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88 / F88M-15     | 2015                                     | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24           | 2021                                     | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3            | 2020 m.                                  | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |
| MDCG 2020-8            | 2020 m.                                  | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                             |
| MDCG 2020-7            | 2020 m.                                  | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                          |
| MDCG 2020-6            | 2020 m.                                  | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                       |

| Nuoroda į standartą | Dabartiniai atitikties / peržiūros metai | Aprašas                                                                                                                                                                                                                                                       |
|---------------------|------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2019-9 v1      | 2022                                     | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                                                                                      |
| MDCG 2019-8 v2      | 2020 m.                                  | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15        | 2020 m.                                  | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11        | 2021                                     | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19        | 2021                                     | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4      | 2021                                     | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2         | 2019                                     | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1         | 2019                                     | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7         | 2018 m.                                  | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6         | 2018 m.                                  | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |
| MDCG 2018-4         | 2018 m.                                  | MDCG 2018-4 Annex: UDI database Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                                                                                                  |

| Nuoroda į standartą  | Dabartiniai atitikties / peržiūros metai | Aprašas                                                                                                                                                                                       |
|----------------------|------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2018-3 v1       | 2020 m.                                  | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25         | 2021                                     | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| MedDEV 2.12-2 2 red. | 2012                                     | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                        |

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3.0 PERŽIŪRŲ ISTORIJA

| SKVDS peržiūros numeris   | Išleidimo data            | Keisti aprašą                                                                | Notifikuotosios įstaigos patvirtinta peržiūra                                                                                                                                                                                                                                                                                                |
|---------------------------|---------------------------|------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022              | 2023 m. sausio mėn. 20 d. | Pirminis leidimas, po MPR CE sertifikavimo                                   | <div>X Taip</div> <div>Patvirtinimo kalba: English</div> <div> <input checked="" type="checkbox"/> Ne (taikoma tik IIa klasės arba kai kurioms IIb klasės implantuojamoms priemonėms (MPR, 52 straipsnio 4 dalies 2 pastraipa), kurių SSCP dar nepatvirtino NB) </div> <div> <input type="checkbox"/> Kita (nurodykite): </div>              |
| SSCP-AS-2023 – 1 peržiūra | 2024 m. kovo 15 d.        | Atnaujinta laikotarpiui nuo 2019 m. sausio 1 d. iki 2023 m. gruodžio 31 d.   | <div>X Taip</div> <div>Patvirtinimo kalba: English</div> <div> <input type="checkbox"/> Ne (taikoma tik IIa klasės arba kai kurioms IIb klasės implantuojamoms priemonėms (MDR 52 straipsnio 4 dalies 2 pastraipa), kurių SSCP dar NB nepatvirtino) </div> <div> <input type="checkbox"/> Kita (nurodykite): </div>                          |
| SSCP-FS-2024 1 peržiūra   |                           | Atnaujinta laikotarpiui nuo 2019 m. rugsėjo 1 d. iki 2024 m. rugpjūčio 31 d. | <div> <input type="checkbox"/> Taip </div> <div>Patvirtinimo kalba: English</div> <div> <input type="checkbox"/> Ne (taikoma tik IIa klasės arba kai kurioms IIb klasės implantuojamoms priemonėms (MDR 52 straipsnio 4 dalies 2 pastraipa), kurių SSCP dar NB nepatvirtino) </div> <div> <input type="checkbox"/> Kita (nurodykite): </div> |

|                            |               |                                                              |                                                                                                                                                                                                                                                                                                                                       |
|----------------------------|---------------|--------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>2 peržiūra | June 20, 2025 | Peržiūrėta remiantis NSAI<br>užklausomis dėl<br>patvirtinimo | <input checked="" type="checkbox"/> Taip<br>Patvirtinimo kalba: English<br><br><input type="checkbox"/> Ne (taikoma tik IIa klasės<br>arba kai kurioms IIb klasės<br>implantuojamoms priemonėms<br>(MDR 52 straipsnio 4 dalies 2<br>pastraipa), kurių SSCP dar NB<br>nepatvirtino)<br><br><input type="checkbox"/> Kita (nurodykite): |
|----------------------------|---------------|--------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|



## Samenvatting van veiligheid en klinische prestaties

### FemoSeal™ Vascular Closure System

|                                                                     |                                                                                            |
|---------------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| <b>Fabrikant</b>                                                    | Terumo Medical Corporation<br>265 Davidson Ave, suite 320<br>Somerset, NJ 08873 VS         |
| <b>SRN van de fabrikant</b>                                         | US-MF-000019594                                                                            |
| <b>Managementvertegenwoordiger/PRRC</b>                             | Kimberly Feitl<br>Vice President, Quality                                                  |
| <b>Basis UDI-DI</b>                                                 | 38970FS79                                                                                  |
| <b>EMDN-nummer</b>                                                  | C900199 – Hemostasesystemen – Overige                                                      |
| <b>Apparaatklasse</b>                                               | Klasse III                                                                                 |
| <b>Jaar waarin het apparaat voor het eerst een CE-markering had</b> | 2005                                                                                       |
| <b>EU-vertegenwoordiger</b>                                         | Terumo Europe N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>België<br>SRN: BE-AR-000001433 |
| <b>Aangemelde instantie</b>                                         | NSAI<br>CE 0050                                                                            |

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Deze samenvatting van de veiligheids- en klinische prestaties (SSCP) is bedoeld om het publiek toegang te bieden tot een bijgewerkte samenvatting van de belangrijkste aspecten van de veiligheid en klinische prestaties van het FemoSeal™ Vascular Closure System (VCS).

Hieronder in **sectie 1.0** volgt een samenvatting van de veiligheids- en klinische prestaties van het apparaat, bedoeld voor gebruikers/zorgprofessionals.

## **1.0 SAMENVATTING VOOR GEBRUIKERS/ZORGPROFESSIONALS**

De SSCP is niet bedoeld als vervanging van de gebruiksaanwijzing als hoofddocument om een veilig gebruik van het hulpmiddel te waarborgen, noch om diagnostische of therapeutische suggesties te geven aan beoogde gebruikers of patiënten. Het SSCP is niet bedoeld als vervanging van de verplichte informatie op de implantaatkaarten of in andere verplichte documenten.

### **1.1 Beoogd gebruik van het apparaat**

#### **1.1.1 Beoogd gebruik**

Het FemoSeal™ Vascular Closure System is een medisch apparaat bestemd voor het sluiten van een arteriële punctie na percutane katheterisatie via de beenslagader.

#### **1.1.2 Gebruiksindicaties**

Het FemoSeal™ Vascular Closure System is geïndiceerd voor gebruik bij het sluiten van de beenslagaderpunctie (arteriotomie) bij patiënten die percutane katheterisatie hebben ondergaan met een 7F (2,33 mm) of kleinere procedurehuls.

#### **1.1.3 Contra-indicaties en/of beperkingen**

FemoSeal™ Vascular Closure System is gecontra-indiceerd bij patiënten met arteriotomieën waarbij hulzen of apparaten groter dan 7F (2,33 mm) zijn gebruikt.

#### **1.1.4 Beoogde patiëntenpopulaties**

De veiligheid en werkzaamheid van het FemoSeal™ Vascular Closure System zijn vastgesteld bij patiënten van 18 jaar en ouder die percutane katheterisatie hebben ondergaan met een 7F (2,33 mm) of kleinere procedurehuls.

#### **1.1.5 Speciale patiëntenpopulaties**

De veiligheid en effectiviteit van het FemoSeal™ Vascular Closure System zijn niet vastgesteld bij de volgende patiëntenpopulaties:

- Patiënten met reeds bestaande auto-immuunziekten.
- Patiënten die therapeutische trombolysen ondergaan.
- Patiënten met klinisch significante perifere vaatziekten.
- Patiënten met ongecontroleerde hypertensie (> 220 mmHg systolisch of > 110 mmHg diastolisch).

- Patiënten met een bloedingsstoornis, waaronder trombocytopenie ( $< 100.000$  bloedplaatjes) of anemie (HgbH  $< 10$  mg/dl).
- Patiënten van wie het binnenlumen van de beenslagader kleiner is dan 5 mm.
- Patiënten met nier- en/of leverfunctiestoornissen.
- Patiënten met andere relevante comorbiditeit.
- Mensen van specifieke raciale en/of etnische afkomst.
- Patiënten met myocardinfarct binnen 72 uur.
- Patiënten met een vasculair transplantaat of stent op het aanprikpunt.
- Zwangere vrouwen of vrouwen die borstvoeding geven.
- Patiënten jonger dan 18 jaar.

### 1.1.6 Beoogd gebruik

De beoogde gebruikers van het FemoSeal™ Vascular Closure System zijn artsen met een opleiding die hen in staat stelt arteriële toegang en sluiting uit te voeren voor endovasculaire procedures via de beenslagader en die hebben deelgenomen aan een instructieprogramma voor artsen van Terumo Medical Corporation FemoSeal™.

## 1.2 Beschrijving van het hulpmiddel

### 1.2.1 Beschrijving van het apparaat

FemoSeal™ Vascular Closure System, vervaardigd door Terumo Medical Corporation (TMC), is een resorbeerbaar vasculair sluitinstrument dat is ontworpen om arteriële hemostase te bereiken na percutane katheterisatie via de beenslagader.

FemoSeal™-sluitelementen bestaan uit twee resorbeerbare polymeerschijven, de binnenafdichting en de buitenste vergrendelschijf, die bij elkaar worden gehouden door een resorbeerbaar multifilament, waardoor de arteriotomie mechanisch wordt afgedicht (zie **Afbeelding 1.1** en **1.2**). Nadat de schijf door de conusbehuizingshuls is ingebracht, wordt de buitenste vergrendelschijf op de multifilamentschacht aangedrukt, wat resulteert in het mechanisch sluiten van het aanprikpunt tussen de binnenste en buitenste vergrendelschijf. De binnenafdichting en de buitenste vergrendelschijf worden op hun plaats gehouden door wrijving op de multifilament-as. Hemostase wordt op mechanische wijze bereikt. De sluitelementen worden aangetast door hydrolyse.

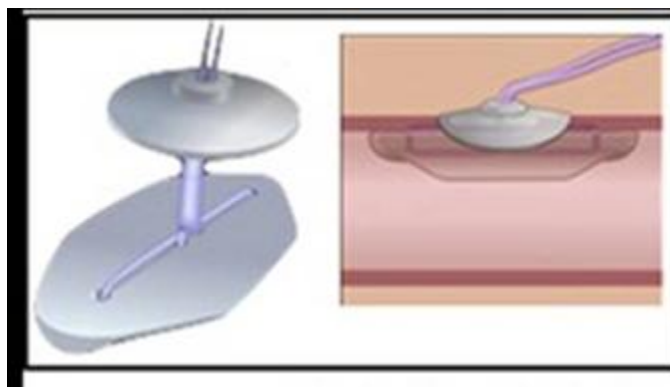
De implanteerbare sluitcomponenten, de binnenafdichting en de buitenste vergrendelschijf worden in achttien (18) maanden tijd afgebroken, terwijl het multifilament naar schatting na twee (2) tot

drie (3) jaar via hydrolyse door het omringende weefsel wordt afgebroken en geresorbeerd. Het vermogen van de implanteerbare sluitcomponenten om compressie op de arteriotomie te handhaven, is tot acht (8) uur getest. De afbraakproducten worden gemetaboliseerd en uitgescheiden in de urine of uitgescheiden als kooldioxide via de longen. In dieronderzoeken zijn geen accumulatie-effecten waargenomen. De extra componenten van FemoSeal™ die tijdens de procedure in contact komen met levend weefsel of bloed zijn de conusbehuizingshuls, dilatator, aandrukhuls, pusher en voerdraad.

**Afbeelding 1.1 Respectievelijk binnenafdichting en buitenste vergrendelschijf**

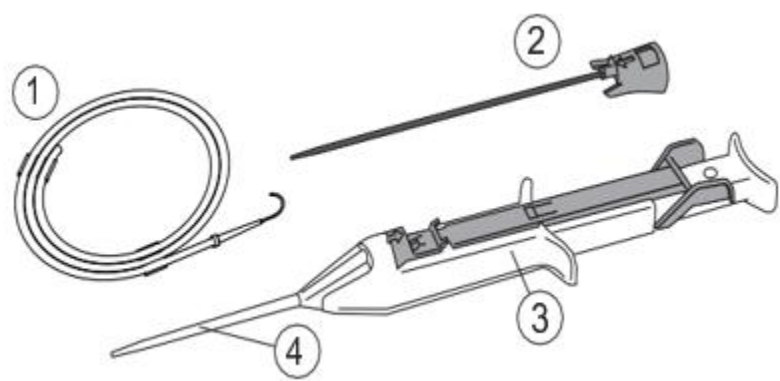


**Afbeelding 1.2 Aangebrachte binnenafdichting en buitenste vergrendelschijf**



De FemoSeal™ unit is verpakt samen met een dilatator en een 0,038" (0,97 mm) OD, 27,5" (70 cm) lange voerdraad en een J-straightener, zie **Afbeelding 1.3** hieronder. De voerdraad bevindt zich in een slang van polyethyleen. Alle onderdelen zijn verpakt in een vaste papieren tray. De verpakking bevat ook de patiëntimplantaatkaart. Voor het FemoSeal™ Vascular Closure System zijn geen extra accessoires nodig om het hulpmiddel naar behoren te laten werken en het hulpmiddel is alleen bedoeld voor gebruik met de dilatator en voerdraad die in de verpakking van het product zijn meegeleverd.

Afbeelding 1.3 FemoSeal™ VCS Unit met voerdraad en dilatator



### 1.2.2 Grondstoffen en componenten

In Tabel 1.1 hieronder staan de componenten van FemoSeal™ VCS.

Tabel 1.1 FemoSeal™ VCS grondstoffen en componenten

| Onderdeelnummer | Beschrijving                                      |                                                               | Materiaal:                                                                                                                                                                                 |
|-----------------|---------------------------------------------------|---------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1               | 0,038" (0,97 mm) voerdraad met een J-straightener |                                                               | Voerdraad: 304 roestvrij staal<br>J-Straightener: Polypropyleen, paars pigment<br>Clip: Polyethyleen<br>Slangen: Polyethyleen                                                              |
| 2               | FemoSeal™ dilatator                               |                                                               | Hub: Tetrahydrofuran, blauw pigment, polybutyleentereftalaat (PBT)<br><br>Slang: Polyethyleen met hoge dichtheid (HDPE), zwart pigment<br><br>Smeermiddel: Silicone Dow Corning 360        |
| 3/4             | FemoSeal-unit                                     | Gegoten RD7 – Binnenafdichting en buitenste vergrendelschijf* | Copolymeer tussen glycolide, trimethyleencarbonaat, ε-caprolacton en TMP: trimethylolpropan (initiator)                                                                                    |
|                 |                                                   | Multifilament *                                               | Gesegmenteerd copolymeer tussen L, L-lactide, trimethyleencarbonaat, ε-caprolacton en 1,3 propaandiol (initiator)<br><br>Coating is copolymeer tussen glycolide, ε-caprolacton en L-lysine |



|  |  |                     |                                                    |
|--|--|---------------------|----------------------------------------------------|
|  |  | Aandrukbuis         | Polypropyleen                                      |
|  |  | Pusher              | 304V roestvrij staal                               |
|  |  | Slider              | Polybutyleentereftalaat (PBT)                      |
|  |  | Behuizing           | Polybutyleentereftalaat (PBT)                      |
|  |  | Toets               | Polybutyleentereftalaat (PBT)                      |
|  |  | Knopdeksel          | Polyoxymethyleen (POM)/polyacetaal copolymeer      |
|  |  | Sleeve              | Polybutyleentereftalaat (PBT)                      |
|  |  | Afstandshouder      | Polybutyleentereftalaat (PBT)                      |
|  |  | Conus               | Polypropyleen                                      |
|  |  | Deksel behuizing    | Polybutyleentereftalaat (PBT)                      |
|  |  | Veiligheidspal      | Polybutyleentereftalaat (PBT), blauw pigment       |
|  |  | Deksel sleeve       | Polybutyleentereftalaat (PBT)                      |
|  |  | Buispakking         | Siliconen wal A 70                                 |
|  |  | Pakking behuizing   | Siliconen wal A 50                                 |
|  |  | Veer                | 302 roestvrij staal                                |
|  |  | Conusbehuizingshuls | Polypropyleen<br>Siliconen Dow Corning 360, hexaan |

\* Implanterbaar deel van het apparaat; implanterbare componenten zijn MRI-veilig

FemoSeal™ VCS is gesteriliseerd met ethyleenoxide (EO) en is een medisch apparaat voor eenmalig gebruik. Het FemoSeal™ VCS-apparaat is zo ontworpen dat het niet opnieuw kan worden gebruikt.

### **Werkingsmodus**

De FemoSeal™ VCS bevordert mechanische hemostase door het inzetten van implanterbare sluitelementen binnen en buiten de beenslagader. Het mechanisme dat bloedingen tegengaat, wordt geleverd door de binnenafdichting die het aanprikpunt afdicht en de buitenste vergrendelschijf die de binnenafdichting op zijn plaats houdt.

#### **1.2.3 Klinisch voordeel**

FemoSeal™ VCS biedt de volgende klinische voordelen met betrekking tot vasculaire sluiting na een beenslagaderpunctie:

- Snellere hemostase<sup>1</sup>
- Minder tijd tot ambulantie<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

#### 1.2.4 Vorige generatie(s) of varianten

- De eerste versie van FemoSeal™ VCS (#11200) werd in de loop van 2005 en een deel van 2006 op de Europese markt verkocht.
- De huidige FemoSeal™ VCS (#11202), met een verbeterd leveringssysteem, is sinds 28 maart 2006 op de markt.

#### 1.2.5 Accessoires die bedoeld zijn voor gebruik in combinatie met het apparaat

De FemoSeal™ unit is verpakt samen met een dilatator, een 0,038" (0,97 mm) OD, 27,5" (70 cm) lange voerdraad en een J-straightener. De voerdraad is een accessoire van de FemoSeal™ unit. De J-straightener is een component van de voerdraad, terwijl de dilatator een component is van de FemoSeal™ unit. De voerdraad is het enige accessoire dat als accessoire wordt beschouwd. De voerdraad bevindt zich in een slang van polyethyleen. Alle onderdelen zijn verpakt in een vaste papieren tray. De verpakking bevat ook de patiëntimplantaatkaart. Voor het FemoSeal™ Vascular Closure System zijn geen extra accessoires nodig om het hulpmiddel naar behoren te laten werken en het hulpmiddel is alleen bedoeld voor gebruik met de dilatator en voerdraad die in de verpakking van het product zijn meegeleverd.

#### 1.2.6 Andere apparaten en producten die bedoeld zijn voor gebruik in combinatie met het apparaat

Voor FemoSeal™ VCS zijn geen extra apparaten nodig om naar behoren te functioneren.

### 1.3 Risico's en waarschuwingen

#### 1.3.1 Restrisico's en ongewenste effecten

Bekende of te verwachten bijwerkingen, letsels en complicaties in verband met het gebruik van het FemoSeal™ VCS als gevolg van restrisico's zijn vermeld in **Tabel 1.2**.

Het voorvalspercentage is gebaseerd op een analyse van de risicodocumentatie en berekend op basis van post-market surveillancegegevens van 1 september 2019 tot en met 31 augustus 2024. Er zijn geen onbekende restrisico's voor het FemoSeal™ VCS en alle van toepassing zijnde risico's zijn afgewikkeld via de gebruiksaanwijzing en het risicobeheerproces.

**Tabel 1.2. Bijwerkingen/complicaties van FemoSeal**

| Letsel                                        | Frequentie (%) | Matigende factoren                                                                                                                                                                    |
|-----------------------------------------------|----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Allergische reacties                          | 0,0000         | In de productontwerpkenmerken, productierichtlijnen, productetikettering en training van artsen is rekening gehouden met acties en plannen om de risico's zo laag mogelijk te houden. |
| Aneurysma                                     | 0,0000         |                                                                                                                                                                                       |
| AV fistel                                     | 0,0001         |                                                                                                                                                                                       |
| Bloedverlies/bloedingen                       | 0,0280         |                                                                                                                                                                                       |
| Overlijden                                    | 0,0002         |                                                                                                                                                                                       |
| Ecchymose                                     | 0,0000         |                                                                                                                                                                                       |
| Embolisme                                     | 0,0000         |                                                                                                                                                                                       |
| Reactie op vreemd lichaam                     | 0,0000         |                                                                                                                                                                                       |
| Hematoom                                      | 0,0027         |                                                                                                                                                                                       |
| Hemorragie                                    | 0,0001         |                                                                                                                                                                                       |
| Infectie                                      | 0,0002         |                                                                                                                                                                                       |
| Ontstekingsreactie                            | 0,0000         |                                                                                                                                                                                       |
| Gevoelloosheid                                | 0,0000         |                                                                                                                                                                                       |
| Pijn                                          | 0,0000         |                                                                                                                                                                                       |
| Ongemak voor de patiënt                       | 0,0004         |                                                                                                                                                                                       |
| Vertraging procedure                          | 0,0065         |                                                                                                                                                                                       |
| Pseudoaneurysma                               | 0,0004         |                                                                                                                                                                                       |
| Retroperitoneale bloeding                     | 0,0002         |                                                                                                                                                                                       |
| Sepsis                                        | 0,0000         |                                                                                                                                                                                       |
| Trombo-embolie                                | 0,0000         |                                                                                                                                                                                       |
| Trombose                                      | 0,0001         |                                                                                                                                                                                       |
| Occlusie bloedvat/ischemie onderste ledematen | 0,0002         |                                                                                                                                                                                       |
| Perforatie van het vat                        | 0,0000         |                                                                                                                                                                                       |
| Dissectie/lacering van vaatweefsel            | 0,0003         |                                                                                                                                                                                       |

### 1.3.2 Waarschuwingen en voorzorgsmaatregelen

#### Waarschuwingen

1. Niet gebruiken als de verpakking beschadigd is of als een steriele barrière niet intact is.
2. Niet gebruiken na de uiterste gebruiksdatum; de biologisch afbreekbare componenten werken mogelijk niet naar behoren.
3. Niet gebruiken als een voorwerp beschadigd of defect lijkt.
4. Infecties kunnen optreden indien het FemoSeal™ Vascular Closure System op plaatsen gebruikt wordt waar bacteriële contaminatie van de procedurehuls of het omringende weefsel kan zijn opgetreden.
5. Als het vermoeden bestaat dat de posterieure arteriële wand is doorboord of als er meer dan één arteriële punctie is gemaakt, vertrouw dan niet alleen op het FemoSeal™ Vascular Closure System om arteriële hemostase te bereiken. Gebruik extra handmatige of mechanische compressie.
6. Als het aanprikpunt zich op of distaal van de bifurcatie van de beenslagader bevindt, mag het FemoSeal™ Vascular Closure System niet worden gebruikt vanwege het risico dat de inwendige afdichting verkeerd wordt gepositioneerd. Dit kan leiden tot bloedingsproblemen en/of verstoring van de normale bloedstroom.
7. Bij aanhoudende arteriële bloeding van de incisieplaats mag het multifilament niet worden doorgesneden totdat hemostase is bereikt. Als er geen hemostase wordt bereikt, bevestigt u het multifilament met een steriel wondverband en oefent u aanvullende compressie uit totdat hemostase is bereikt. Bij aanhoudende arteriële bloedingen kunnen aanzienlijke bloedingscomplicaties optreden die letsel of overlijden van de patiënt tot gevolg kunnen hebben.
8. Gebruik het FemoSeal™ Vascular Closure System niet als het aanprikpunt proximale van het liesligament ligt, omdat dit kan leiden tot retroperitoneaal hematoom.
9. Patiënten met een hoger risico op bloedingen kunnen meer bloed verliezen, waardoor een transfusie nodig is.
10. Als de binnenschijf losraakt, kan dit mogelijk een trombotische en/of embolische gebeurtenis veroorzaken.

#### Voorzorgsmaatregelen

1. De plaatsingsprocedure van het FemoSeal™ Vascular Closure System moet worden uitgevoerd door artsen met adequate training in het gebruik van het apparaat.
2. Voer een beperkt femoraal angiogram of een echografisch geleide femorale punctie uit voorafgaand aan de plaatsing van het FemoSeal™ Vascular Closure System.

3. Stop de procedure als:
  - De lumendiameter van de beenslagader < 5 mm is.
  - Stenose en/of significante plaque aanwezig is in de nabijheid van de het aanprikpunt in de beenslagader.
  - Arteriële punctie ter hoogte van, of distaal van de femorale arterie-bifurcatie plaatsvindt.
  - Afwijkende vertakkingen of afwijkingen in het bloedvat die aanwezig zijn in de nabijheid van het aanprikpunt in de beenslagader.
4. Als er een hematoom aanwezig is, moet extra zorg worden besteed aan het correct inbrengen van de conusbehuizingshuls in de arterie.
5. Gebruik een enkele wandsteektechniek. Steek de posterieure wand van de arterie niet door.
6. Neem te allen tijde de steriele manier in acht wanneer u het FemoSeal™ Vascular Closure System gebruikt.
7. Het FemoSeal™ Vascular Closure System is uitsluitend voor eenmalig gebruik en mag op geen enkele wijze opnieuw worden gesteriliseerd of gebruikt. De FemoSeal™ unit is zo ontworpen dat deze niet opnieuw kan worden gebruikt.
8. Als de binnenafdichting onverwacht weerstand ondervindt, moet de procedure worden gestaakt.
9. Om de binnenafdichting correct te plaatsen, moet u uw duim zo verplaatsen dat de knop vrij kan terugveren.
10. Zorg ervoor dat de punt van de conusbehuizingshuls van de FemoSeal™ Unit zich onder het huidoppervlak bevindt voordat de buitenste vergrendelschijf wordt geplaatst. De buitenste vergrendelschijf kan onbedoeld boven huidniveau worden geplaatst bij patiënten met een korte afstand tussen de beenslagader en het huidniveau.
11. Voor een correcte plaatsing kan een incisie in de huid nodig zijn vóór de plaatsing.
12. Als de binnenafdichting zich in de arterie bevindt, maar het niet mogelijk is om de knop volledig in te drukken en de buitenste vergrendelschijf te plaatsen, kan een operatie nodig zijn om de FemoSeal™-sluitelementen te verwijderen.
13. Indien binnen 18 maanden een nieuwe punctie van dezelfde beenslagader nodig is, moet een nieuwe punctie worden uitgevoerd op ten minste één centimeter proximaal van de vorige toegangsplaats van het FemoSeal™ Vascular Closure System.
14. Instrueer de patiënt om de instructies van de arts met betrekking tot de inspectie van de sluitingsplaats op te volgen.

15. Instrueer de patiënt om de patiëntinformatiekaart voor de komende 18 maanden bij zich te dragen

### **Voorzorgsmaatregelen ten tijde van het ontslag**

Beoordeel de patiënt op de volgende klinische condities voordat u overweegt hem/haar te ontslaan:

1. Bloeding en/of hematoom op de sluitingsplaats.
2. Pijn tijdens het lopen.
3. Teken van infectie op de sluitingsplaats.

### **1.3.3 Corrigerende veiligheidsmaatregelen**

In de periode 1 september 2019 tot en met 31 augustus 2024 is er één corrigerende actie in verband met de veiligheid van FemoSeal™ VCS uitgevoerd.

In 2022 heeft Terumo het FemoSeal™ VCS vrijwillig teruggeroepen vanwege klachten over de fouten in de proces- en partijvrijgavetests van het door Elkton vervaardigde FemoSeal-product voor de meting van de opvulkracht en de terugtrekkracht. In totaal werden 950 eenheden uit Zuid-Korea teruggeroepen.

## **1.4 Klinische evaluatie en klinische follow-up na het op de markt brengen**

**Tabel 1.3** bevat een lijst van centrale studies die zijn opgenomen om FemoSeal™ VCS op de markt te brengen, evenals post-market studies en post-market klinische follow-up activiteiten. De versie van het apparaat dat in het onderzoek wordt gebruikt, is in de onderstaande tabel opgenomen. De eerste versie van FemoSeal™ VCS (#11200) was tot 2006 op de markt; de volgende versie (#C11202) werd geïntroduceerd in 2006. Dit is tevens de versie die momenteel op de markt is.

**Tabel 1.3 Samenvatting van centrale onderzoeken**

| <b>Functionele dierproeven vóór het op de markt brengen</b>                                                                                                                                                                                                             | <b>Apparaatversie</b> |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                 |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                 |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                 |

| <b>Eerste klinische studie bij mensen</b>                                                                                                                                                                    |                          |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 11200                    |
| <b>Voltooide post-market klinische onderzoeken</b>                                                                                                                                                           |                          |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                   | C11202 (huidig apparaat) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                            | C11202 (huidig apparaat) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                                                                                               | C11202 (huidig apparaat) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)                                                                                       | C11202 (huidig apparaat) |
| <b>Geplande/lopende klinische onderzoeken na het op de markt brengen</b>                                                                                                                                     |                          |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                                                                                                   | C11202 (huidig apparaat) |
| <b>Klinische follow-upactiviteiten na het op de markt brengen</b>                                                                                                                                            |                          |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                                                                                                    | C11202 (huidig apparaat) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                                                                                                           | C11202 (huidig apparaat) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024)                                                                              | C11202 (huidig apparaat) |

### 1.4.1 Samenvatting van gegevens van pre-market (dierproeven en klinische onderzoeken)

**Tabel 1.4** hieronder beschrijft alle pre-market studies, zowel dierproeven als klinisch onderzoek.

**Tabel 1.4 Samenvattingen van pre-market studies**

| <b>Functionele dierproeven vóór het op de markt brengen</b>                                                                                                                                                                 |                                                                            |                                         |                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                           |
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| <b>Naam van het onderzoek</b>                                                                                                                                                                                               | <b>Jaar / CI</b>                                                           | <b>Type onderzoek</b>                   | <b>Doelen</b>                                                                                                                                                                                                                                    | <b>Mijlpalen</b>                                                                                                                                                                                                                                                     | <b>Criteria voor potentiële acceptatie</b>                                                                                                                                                                                                                                                                                                                                                                |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical | 2000<br>Radi Medical System AB<br><br>Uitgevoerd door Biomatech, Frankrijk | Dier-onderzoek;<br>Verkenkend onderzoek | Het doel van het onderzoek was het evalueren van de biocompatibiliteit en biofunctionaliteit van een biologisch afbreekbaar implantaat dat is ontworpen om hemostase in het vasculaire systeem te bereiken.<br>Rapportadressen reservedieren van | N = 3 volwassen vrouwelijke schapen, 1 dier per tijdstip<br><br>Follow-up voor histopathologische analyse, macroscopische indeling en ultrastructurele analyse<br><br><ul style="list-style-type: none"> <li>• 12 mnd</li> <li>• 15 mnd</li> <li>• 18 mnd</li> </ul> | Arteriële doorgankelijkheid <ul style="list-style-type: none"> <li>• Beoordeling van de bloedstroom na plaatsing – 2/3 vermindering van de bloedstroom in verband met tijdelijk arterieel vasospasme dat werd toegeschreven aan de ingreep, beide traden op bij de linker arteria carotis communis</li> <li>• Ultrasonische beoordeling met kleurendoppler (4 weken) - 3/3 (100%) zonder grote</li> </ul> |

|                                             |  |  |                                            |                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
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| System AB (performed by Biomatech, France). |  |  | onderzoeksnummer 862 (documentnr. 1051-01) | <p>Ultrasonie controle met kleurendoppler. 30 dagen op carotis- en femorale arteriële toegangslocaties</p> | <p>vermindering van de bloedstroom 30 dagen na implantatie</p> <p>Macroscopische waarnemingen</p> <ul style="list-style-type: none"> <li>12 maanden – macroscopisch bevestigde doorgankelijkheid zonder anatomisch zichtbare occlusie; geen macroscopische lokale intolerantelaesies (hemorragie, necrose of neovascularisatie); inkapseling van interne discus bleek te zijn gemarkeerd</li> <li>15 maanden – macroscopische observatie vertoonde geen tekenen van ontsteking; geen residuen van binnen- of buitenschijven waargenomen; inkapselingsweefsel in het gebied van de buitenschijf leek hetzelfde als bij de 12 maanden-observatie</li> <li>18 maanden – macroscopische observatie toonde geen tekenen van lokale intolerantie, buitenste schijf zichtbaar (3/3 gevallen), afbraak van binnenschijf volledig; 1/3 (linker arteria carotis communis) - depressie van arteriewand waargenomen op implantatieplaats (kan gerelateerd zijn aan plaatsing van het apparaat)</li> </ul> <p>Conclusies</p> <ul style="list-style-type: none"> <li>Macroscopisch, bij 12, 15 en 18 maanden na implantatie werden geen necrotische, degeneratieve of trombotische tekenen gedetecteerd.</li> <li>Het afbraakproces van de binnenste en buitenste schijf bleek tussen 12 en 18 maanden te verlopen en voltooid te zijn na 18 maanden, waarbij een</li> </ul> |
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|                                                                                                                                                                                                                                                                                |                                                                                |                                             |                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                 | <p>witachtig weefsel het geïmplanteerde gebied bedekte.</p> <ul style="list-style-type: none"> <li>Histologisch gezien was polymateriaal na 18 maanden niet meer zichtbaar, maar was er een endoluminaal fibreus weefsel aanwezig. Er zijn geen necrotische, degeneratieve of trombotische laesies waargenomen.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002 Radi Medical System AB</p> <p>Uitgevoerd door Biomatech, Frankrijk</p> | <p>Dier-onderzoek; Verkennend onderzoek</p> | <p>Het doel van het onderzoek was het evalueren van de biocompatibiliteit van een biologisch afbreekbaar implantaat dat geschikt was om hemostase in het vasculaire systeem te bereiken.</p> | <p>Follow-up (na implantatie)</p> <ul style="list-style-type: none"> <li>12 weken</li> <li>24 weken</li> <li>36 weken</li> </ul> <p>N = 12 schapen, 3 dieren per tijdstip, 3 reservedieren gedood op 12, 15 en 18 maanden</p> <p>Implantatieplaatsen – rechter en linker beenslagaders, rechter en linker arteria carotis communis</p> <p>Ultrasonische kleurdoppleranalyse</p> | <p><u>Doorgankelijkheid van arteria carotis en femoralis na 4 weken</u></p> <ul style="list-style-type: none"> <li>Grote vermindering van de bloedstroom 0/12 (0%)</li> </ul> <p><u>Geen grote vermindering van de bloedstroom</u></p> <ul style="list-style-type: none"> <li>Ernstige beperking van de bloedstroom in verband met het inbrengen van het apparaat 0/12 (0%)</li> <li>Vermindering van de bloedstroom in linker arteria carotis 2/12 (16,6%) als gevolg van tijdelijk arterieel vasospasme (toegewezen aan de operatie, niet aan het apparaat)</li> </ul> <p><u>Beschadiging van de bloedstroom door follow-up</u></p> <p>12 weken – 0/12 (0%)</p> <p>24 weken – 0/12 (0%)</p> <p>36 weken – 0/12 (0%)</p> <p>Bloeddrukmetingen (3 schapen – 36 weken)</p> <ul style="list-style-type: none"> <li>Geen grote vermindering van de bloedstroom gedetecteerd</li> </ul> <p>Macroscopische gegevens voor integratie en afbraak (graad 0-4)</p> |

|  |  |  |  |  | <u>Carotis locaties</u><br><i>Intern</i><br>-inkapseling<br>12 weken 1,3<br>24 weken 0,8<br>36 weken 0,7<br>-materiaalafbraak<br>12 weken 2,2<br>24 weken 2,3<br>36 weken 0,7<br><i>Extern</i><br>-inkapseling<br>12 weken 2,0<br>24 weken 1,0<br>36 weken 0,8<br>-materiaalafbraak<br>12 weken 2,0<br>24 weken 2,7<br>36 weken 3,2<br><br><u>Femorale locaties</u><br><i>Extern</i><br>-inkapseling<br>12 weken 1,0<br>24 weken 2,7<br>36 weken 1,0<br>-materiaalafbraak<br>12 weken 2,0<br>24 weken 2,4<br>36 weken 3,0<br><br><i>Intern</i><br>-inkapseling<br>12 weken 2,0<br>24 weken 1,2<br>36 weken 1,0<br>-materiaalafbraak<br>12 weken 1,0<br>24 weken 2,2<br>36 weken 3,0<br><br><u>Histologische gegevens voor integratie-, afbraak- en inflammatoire parameters (gemiddelde van relevante waarden, index 0-4) n=6</u><br><br><u>Carotis locaties</u><br>Externe fibrose<br>12 weken – 2,3<br>24 weken – 2,3 |
|--|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | 36 weken – 1,8<br>Interne neo-intima<br>12 weken – 3,0<br>24 weken – 2,7<br>36 weken – 3,3<br>Afbraak van materiaal<br>12 weken – 1,7<br>24 weken – 3,0<br>36 weken – 3 +<br>Inflammatoire parameters<br>(macrofagen)<br>12 weken – 3,0<br>24 weken – 1,7<br>36 weken – 1,7<br><u>Femorale locaties</u><br>Externe fibrose<br>12 weken – 1,3<br>24 weken – 1,5<br>36 weken – 1,7<br>Interne neo-intima<br>12 weken – 3,7<br>24 weken – 3,3<br>36 weken – 3,8<br>Afbraak van materiaal<br>12 weken – 2,0<br>24 weken – 3,0<br>36 weken – 3+<br>Inflammatoire parameters<br>(macrofagen)<br>12 weken – 3,5<br>24 weken – 1,8<br>36 weken – 1,8<br><br><u>Histomorfologische<br/>doorgankelijkheid</u><br>Carotis locaties<br>12 weken 74,0%<br>24 weken 81,9%<br>36 weken -89,43%<br>Femorale locaties<br>12 weken – 42,2%<br>24 weken – 73,21%<br>36 weken – 78,71%<br><br><u>VS vaatdoorgankelijkheid<br/>(gemiddeld %)</u><br>Carotis locatie<br>12 weken 94,6%<br>24 weken – 96,7%<br>36 weken – 94,7%<br>Femorale locaties |
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|                                                                                                                                                                                                                                                                 |                                                                                |                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                            | 12 weken – 66,9%<br>24 weken – 63,6%<br>36 weken – 75,1%<br><br>Conclusies <ul style="list-style-type: none"> <li>• Er werd geen significant lokaal intolerantiesignaal gedetecteerd (afwezigheid van zichtbare inflammatoire, necrotische of degeneratieve laesies) na 12, 24 of 36 weken</li> <li>• Er werd geen significante ongewenste tissulaire reactie geregistreerd met betrekking tot de gastheer en het apparaat</li> <li>• Degradatie van het implantaat was bijna voltooid na 36 weken</li> </ul>                                                                                                                                                                |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France). | 2002<br><br>Radi Medical System AB<br><br>Uitgevoerd door Biomatech, Frankrijk | Dier-onderzoek | Het doel van het onderzoek was het evalueren van de biocompatibiliteit en biofunctionaliteit van een biologisch afbreekbaar implantaat dat is ontworpen om hemostase in het vasculaire systeem te bereiken. Het geteste hulpmiddel was bestemd om in de punctieopening in de slagaders te komen om hemostase te bereiken. De ene schijf wordt in de punctieopening in de slagader gebracht en de andere schijf vergrendelt de binnenschijf van buiten de slagader. Beide schijven werden ingebracht via een inbrenghuls. De schijven zijn ontworpen om bloedingen te voorkomen, in de vaatwand te genezen en uiteindelijk af te breken en te worden geabsorbeerd. Het onderzoek werd | Implantatieperiode / follow-up is 5 weken voor alle dieren<br><br>4 schapen, 1 varken<br><br>14 sluitelementen<br><br>8 sluitelementen geïmplanteerd in 2 schapen,<br><br>2 sluitelementen geïmplanteerd in 1 varken<br><br>Wanneer twee sluitelementen in dezelfde dijbeenslagader werden geïmplanteerd, zijn ze geïmplanteerd op een afstand van > 30 mm | Alle criteria voor bijwerkingen (ontsteking, necrose, bloeding of andere laesies) of elke dunne pseudo-intimale laagvorming werden geregistreerd. Er werd bijzondere aandacht besteed aan de eerste tissulaire integratie van het apparaat, met speciale nadruk op de interne schijfinkapseling.<br><br>Macroscopisch werden geen significante tekenen van lokale intolerantie of trombusvorming waargenomen. Uit de macroscopische observatie bleek geen verschil tussen het schaap of het varken na implantatie van de sluitelementen in de dijbeenslagaders. Macroscopisch werden geen significante tekenen van lokale intolerantie of trombusvorming waargenomen. Uit de |

|  |  |  | ontwikkeld om gegevens te verzamelen en te analyseren na functionele implantatie bij schapen en varkens om het vermogen van het implantaat te evalueren om de fysiologische functie te behouden bij gebruik in het bloedsomloopstelsel, om de respons van de gastheer en de respons van het hulpmiddel te bepalen (fysieke integriteit, tissulaire inkapseling bij opoffering) en om de afbraak van het implantaat te evalueren |  | <p>macroscopische observatie bleek geen verschil tussen het schaap of het varken na implantatie van de sluitelementen in de dijbeenslagaders.</p> <p>De histopatologische analyse van de implantatieplaats bij schapen toonde geen lokale bijwerkingen aan. De binnenste en buitenste schijven vertoonden tekenen van degradatie en werden in sommige gevallen in kleinere delen gebroken. De binnenste schijven werden volledig geïntegreerd in neo-intimaal weefsel. Bij het varken vertoonde de histopatologische analyse iets meer inflammatoire tekenen rond de binnenste en buitenste schijven. Bij beide dieren vertoonde het multifilament iets meer inflammatoire tekenen dan in het schijfmateriaal, wat normaal is voor gevlochten hechtdraden vanwege het grotere oppervlak.</p> <p>De doorgankelijkheid van het bloedvat werd na 5 weken gemeten met behulp van drie verschillende methoden, histomorfometrisch, histomorfometrisch in combinatie met meting van de vaatlumina met behulp van een schuifmaat en met behulp van een kleurendoppler-echografie. De gemiddelde vaatdoorgankelijkheid bij schapen lag tussen 60 en 80%, afhankelijk van de</p> |
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|                                                                                                                                                                                                              |                              |                                           |                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                           | methode (12 waarnemingen). Bij het varken lag de gemiddelde vaatdoorgankelijkheid tussen 40 en 80% (2 waarnemingen).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
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| <b>Eerste klinische studie bij mensen</b>                                                                                                                                                                    |                              |                                           |                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Naam van het onderzoek                                                                                                                                                                                       | Jaar / CI                    | Type onderzoek                            | Doelen                                                                                                                                                                                                                                                                                                                                                               | Mijlpalen                                                                                                                                                                                                                                                                                                                                                                                 | Criteria voor potentiële acceptatie                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Open label, enkele arm, multi-centre test | De doelstellingen van het onderzoek waren het bepalen van de veiligheid, prestaties en effectiviteit van het FemoSeal Vascular Closure System (FemoSeal Systeem) in het algemeen, en in het bijzonder de sluitelementen, bij patiënten die cardiale diagnostische of interventionele cardiologische procedures ondergaan met behulp van toegang tot de beenslagader. | <p>2-delige studie</p> <p>Totaal n = 80</p> <p>Deel 1 n = 20</p> <p>Deel 2 n = 60</p> <p>Indicaties:</p> <p>Deel 1 – diagnostische cardiale katheterisatie met behulp van de beenslagader als toegangslocatie</p> <p>Deel 2 – Patiënten die diagnostische en interventionele hartprocedures ondergaan met behulp van de beenslagader als toegangslocatie</p> <p>Follow-up na 30 dagen</p> | <p>Uitkomsten</p> <p><u>hemostase bereikt met FS zonder compressie</u></p> <p>- Deel 1 20/20 (100%)</p> <p>- Deel2 58/60 (97%)</p> <p>Mediane tijd tot hemostase op het moment van de ingreep (deel 2) - 1,0 minuut (bereik onmiddellijk – 8 minuten)</p> <p><u>Tijd tot ambulantie (minuten)</u></p> <p>Deel 1 –</p> <p>Mediaan: 33,0</p> <p>gemiddeld: 67,8</p> <p>Deel 2 –</p> <p>mediaan: 45</p> <p>gemiddeld: 87,5</p> <p><u>Incidentie van ernstige vasculaire complicaties – follow-up na 30 dagen</u></p> <p>Deel 1</p> <p>-Vrij van vasculaire complicaties 20/20 (100%)</p> <p>Deel 2</p> <p>Pseudoaneurysma – 1/59 (1,69%)</p> <p><u>Behandeling mislukt</u></p> <p>Deel 1 – 0/20 (0%)</p> <p>Deel 2 – 3/60 (5%)</p> <ul style="list-style-type: none"> <li>2 vanwege het niet bereiken van hemostase zonder</li> </ul> |

|  |  |  |  |  | gebruik van compressie <ul style="list-style-type: none"> <li>1 vanwege ernstige vasculaire complicatie, pseudo-aneurysma</li> </ul> |
|--|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <u>Blijvend slijpelen van bloed</u><br>Deel 1 – 0/20 (0%)<br>Deel 2- 8/60 (13%)                                                      |
|  |  |  |  |  | <u>Hematoom</u><br>Deel 1 – 0/20 (0%)<br>Deel 2 – 6/60 (10%)                                                                         |

In het kader van het pre-marketontwikkelingsplan voor FemoSeal™ VCS werden drie functionele dierproeven uitgevoerd. In 2000 werd, voorafgaand aan de start van klinische studies, een dieronderzoek uitgevoerd om de biofunctionaliteit van FemoSeal™ VCS te evalueren. Dit onderzoek evalueerde het vermogen van de sluitelementen om de fysiologische functie te behouden en de afbraak ervan te evalueren. Na 18 maanden was het materiaal van de binnen- en buitenschijf niet meer zichtbaar, maar vervangen door een endoluminaal fibreus weefsel. Tot slot werd bevestigd dat het FemoSeal™ VCS-sluitelement in staat is om de fysiologische functie te handhaven wanneer het in de bloedsomloop wordt gebruikt.

In 2002 werd een dierproef uitgevoerd om de biocompatibiliteit en biofunctionaliteit van een biologisch afbreekbaar implantaat, namelijk FemoSeal™ VCS, te evalueren, dat ontworpen is om hemostase in het vasculaire systeem te bereiken. Samengevat was de degradatie van het implantaat na 36 weken bijna voltooid en vond er geen significante nadelige tissulaire reactie plaats.

Een andere dierproef in 2002 evalueerde de biocompatibiliteit en biofunctionaliteit van een biologisch afbreekbaar implantaat, namelijk FemoSeal™ VCS, dat ontworpen is om hemostase in het vasculaire systeem te bereiken. Na 5 weken was de inkapseling van de schijf voltooid en werden tekenen van afbraak waargenomen van de binnen- en buitenschijf. Tot slot werd bevestigd dat het implantaat in staat is de fysiologische functie te behouden wanneer het in de bloedsomloop wordt gebruikt.

Als onderdeel van het klinische ontwikkelingsplan voor FemoSeal™ VCS heeft Radi Medical System AB een klinisch onderzoek uitgevoerd vóór het op de markt brengen. Dit klinisch onderzoek is niet gepubliceerd of online beschikbaar. Het onderzoek met hulpmiddelmodel

#11200 werd uitgevoerd in 2002-2004 volgens de Europese norm EN 540 (Klinisch onderzoek naar medische hulpmiddelen voor mensen) en in overeenstemming met de algemene overwegingen voor klinische proeven van ICH en de richtlijn voor goede klinische praktijken. De details van dit onderzoek worden gedocumenteerd in het verslag EU-SE-001. Het klinische onderzoek werd vastgelegd in het eindverslag van Radi Medical Systems AB, "Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures". Het klinische onderzoek werd uitgevoerd met FemoSeal's eerste model #11200 en was gericht op de veiligheid en effectiviteit van de implanteerbare sluitcomponenten. Het enige verschil tussen het eerste model #11200 en het huidige model, C11202, is respectievelijk de Franse grootte, 6F en 7F, en het verbeterde afgiftesysteem. De klinische voordelen, het beoogde gebruik, de werkingsprincipes en de grondstoffen van de implanteerbare sluitelementen, de binnenafdichting en de buitenste vergrendelschijf blijven ongewijzigd.

Het beoogde gebruik van het apparaat was voor patiënten die diagnostische cardiale of interventionele cardiale procedures ondergingen waarbij de beenslagader als toegangspunt werd gebruikt. Het doel van dit onderzoek was het bepalen van de veiligheid, prestaties en effectiviteit van FemoSeal™ VCS. Dit was een prospectief, multicenter, open-label, eenarmig onderzoek en follow-up na 30 dagen.

Het primaire prestatie-eindpunt was de tijd tot hemostase, gedefinieerd als het ontbreken van hevige bloedingen. Het primaire veiligheidseindpunt was de incidentie van ernstige vasculaire complicaties gedurende 30 dagen. Secundaire eindpunten waren de tijd tot ambulantie, het percentage mislukte behandelingen, de incidentie van ongewenste voorvallen en de prestatiekenmerken van het apparaat tijdens de toediening en implementatie.

Patiënten die aan dit onderzoek deelnamen, waren volwassenen die geïnformeerde toestemming konden geven en die ten minste één intacte pulsatie aan de voeten hebben. Patiënten werden uitgesloten van het onderzoek als ze een van de volgende aandoeningen hadden:

- Voorgeschiedenis van perifere vasculaire aandoeningen
- Auto-immuunziekten
- Bekende bloedingsstoornis van ernstige anemie
- INR >1,5
- Myocardinfarct met 72 uur
- Ongecontroleerde hypertensie ondanks behandeling
- Obesitas die toegang onmogelijk maakt met de Seldinger-techniek
- Aanwezigheid van vasculaire graft of stent op arteriotomieplaats



- Eerdere ipsilaterale punctie binnen 3 maanden
- Levensduurverwachting < 6 maanden

Daarnaast werden patiënten intraoperatief onderzocht en uitgesloten van het onderzoek als een van de volgende situaties werd waargenomen:

- Lumendiameter van beenslagader van <5 mm
- Arteriële takken binnen 2 cm proximaal van het aanprikpunt
- Significante stenose binnen 3 cm van het aanprikpunt
- Gebruik van de primaire inbrenghuls >6 Fr
- Punctie bij of distaal van femorale bifurcatie
- Meerdere femorale puncties
- Bekende of vermoede perforatie van de posterieure femurwand
- Groot hematoom (2:6 cm) na voltooiing van de procedure
- Moeilijke primaire inbrenging van de huls voor de ingreep als gevolg van kronkelig weefsel of bloedvat

Dit onderzoek met één enkel protocol werd in twee delen uitgevoerd: Aan deel 1 namen 20 patiënten deel, waarna er een veiligheidsanalyse werd uitgevoerd. Daarna namen er nog eens 60 patiënten deel aan deel 2.

In deel 1 was de gemiddelde leeftijd van de deelnemende patiënten 65,9 jaar, 70,0% van de patiënten was man en 95% van de patiënten had gelijktijdig medicatie. In deel 2 van het onderzoek was de gemiddelde leeftijd 63,8 jaar, 78% was man en 100% had gelijktijdig medicatie.

Patiënten die diagnostische (deel 1 en deel 2) of interventionele (deel 2) cardiale katheterisatieprocedures ondergingen, kwamen in aanmerking voor deelname aan het onderzoek. De procedures voldeden aan de zorgstandaard in elk van de deelnemende ziekenhuizen, gevolgd door het gebruik van FemoSeal™ VCS. Patiëntgegevens werden verzameld bij de baseline, tijdens de procedure en 1 dag en 30 dagen na de procedure. De resultaten zijn samengevat in **Tabel 1.5** en geven aan dat FemoSeal™ VCS veilig en effectief is voor gebruik bij deze patiëntenpopulatie.

**Tabel 1.5 Klinische resultaten gerapporteerd in de pre-market studie**

|                                                                                                                            | Deel 1       | Deel 2                    |
|----------------------------------------------------------------------------------------------------------------------------|--------------|---------------------------|
| Aantal patiënten                                                                                                           | 20           | 60                        |
| Gemiddelde tijd tot hemostase                                                                                              | 1,2 minuten  | 1,6 minuten <sup>a</sup>  |
| Gemiddelde tijd tot ambulantie                                                                                             | 72,2 minuten | 87,5 minuten <sup>b</sup> |
| Incidentie van ernstige vasculaire complicaties <sup>c</sup>                                                               | 0 (0%)       | 1 (2%)                    |
| Aantal patiënten met bijwerkingen                                                                                          | 5 (25%)      | 19 (32%)                  |
| Falen van de behandeling (gedefinieerd als ernstige vasculaire complicaties, noodzaak tot handmatige compressie, of beide) | 0 (0%)       | 3 (5%)                    |
| Storingen in het apparaat                                                                                                  | 0 (0%)       | 6 (10%)                   |

<sup>a</sup> Gebaseerd op een totale steekproefomvang van 58, omdat 2 patiënten ten tijde van de procedure geen hemostase bereikten vanwege eerdere ipsilaterale puncties. Hemostase werd bereikt na 7 minuten en 37 minuten voor deze patiënten.

<sup>b</sup> Op basis van de totale steekproefgrootte van 59: 1 patiënt werd niet meegerekend omdat deze werd beademd vanwege longoedeem en langer dan een week niet ambulant was.

<sup>c</sup> Gedefinieerd als vasculaire complicatie die bloedtransfusie of chirurgisch herstel vereist, of lokale infectie die toediening van antibiotica, een (verlenging van de) ziekenhuisopname of débridement van de locatie vereist

In deel 1 van het onderzoek werden geen ernstige vasculaire complicaties waargenomen. Er werd één ernstige vasculaire complicatie gemeld in deel 2 van het onderzoek: pseudo-aneurysma dat binnen één dag na de ingreep werd gemeld. Het voorval vereiste echografisch geleide compressie en een injectie van trombine in het pseudo-aneurysma en verlengde de ziekenhuisopname van de patiënt.

Van de vijf bijwerkingen die in deel 1 van het onderzoek werden gemeld, was er één mogelijk aan het apparaat gerelateerde bijwerking: een niet-ernstig voorval van een klapbloeding 1 dag na de procedure. Van de 19 bijwerkingen die in deel 2 van het onderzoek werden gemeld, werden drie aan het apparaat gerelateerde niet-ernstige bijwerkingen van hematoom waargenomen, en er werden zes mogelijk aan het apparaat gerelateerde niet-ernstige voorvallen waargenomen, waaronder drie meldingen van aanhoudend sijpelen, twee hematomen en één keer beenpijn na lichaamsbeweging.

Er waren 3 patiënten in deel 2 die als behandelingsfouten werden beschouwd: 2 vanwege het niet bereiken van hemostase zonder het gebruik van compressie en 1 vanwege de ernstige vasculaire

complicatie (pseudo-aneurysma). In deel 1 van het onderzoek waren er geen mislukte behandelingen.

Van de zes apparaatstoringen in deel 2 van het onderzoek hadden er drie geen invloed op de procedure, één was toe te schrijven aan een gebruikersfout, één was een lekkage van de introducer en één was een gebroken filamentverbinding. De laatste twee problemen werden aangepakt met modelupdates die in C11202 werden geïmplementeerd.

Deel 2 van de pre-market klinische studie rapporteerde de resultaten van de follow-up na 6 maanden niet wegens niet-naleving door de patiënt. De resultaten van de pre-market klinische studie (EU-SE-001) van 30 dagen, die in overeenstemming zijn met de follow-upperiode van de klinische literatuur, tonen aan dat FemoSeal™ VCS veilig en effectief is.

### 1.4.2 Samenvatting van gegevens uit klinische post-market onderzoeken

Er zijn vier voltooide klinische onderzoeken na het in de handel brengen die in onderstaande **Tabel 1.6** worden beschreven. Deze klinische onderzoeken zijn niet gepubliceerd of online beschikbaar.

**Tabel 1.6 Post-market klinische onderzoeken**

| Voltooide post-market klinische onderzoeken                                                 |                              |                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                    |
|---------------------------------------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Naam van het onderzoek                                                                      | Jaar / CI                    | Type onderzoek                                                          | Doelen                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Mijlpalen                                                                                                                                                                                                                                                                                                                                                      | Criteria voor potentiële acceptatie                                                                                                                                |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI                 | Post-market onderzoek, acceptatie van nieuwe verpakking door gebruikers | Post-market studie uitgevoerd op het nieuwere model FemoSeal Vascular® Closure System #11202 dat een aangepast plaatsingssysteem heeft ten opzichte van het eerste model, #11200, om de functionaliteit te documenteren.<br><br>Het doel van het onderzoek was om feedback te krijgen over de herziene gebruiksaanwijzing (IFU), het opleidingsproject voor artsen en verpleegkundigen, om de beoordelingen in de risicoanalyse te bevestigen en input te geven voor eventuele verbeteringen van de productkwaliteit. | 100 patiënten <ul style="list-style-type: none"> <li>63 mannen / 37 vrouwen</li> <li>Gemiddelde leeftijd 68 jaar voor vrouwen, 65 jaar voor mannen</li> </ul> 2 Zweedse ziekenhuizen, 6 artsen<br><br>112 apparaten<br><br>Gegevens vastgelegd op patiëntendossierformulieren (CRF)<br><br>Geplande observatietijd: 30 minuten vanaf het moment van toepassing | Uitkomsten<br><br>1. Illustraties/instructies in de gebruiksaanwijzing die als informatief en adequaat worden beschouwd<br><br>2. Onmiddellijke hemostase (91/100) |
| Confirmatory Assessment of FemoSeal™ Vascular                                               | Dr. Nicolas Moes<br>Medische | Post-market bevestigende beoordeling                                    | Het doel van dit onderzoek was het beoordelen van de veiligheid en prestaties van                                                                                                                                                                                                                                                                                                                                                                                                                                     | 50 opeenvolgende patiënten                                                                                                                                                                                                                                                                                                                                     | Primaire eindpunten <ul style="list-style-type: none"> <li>Primair werkzaamheidseindpunt: TTH (tijd tot hemostase)</li> </ul>                                      |

|                                                                                |                                    |                       |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
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| Closure System in 7F-Sheath. (2008)                                            | Universiteit Innsbruck, Oostenrijk |                       | FemoSeal® die tijdens de normale klinische routine werd gebruikt bij patiënten die een diagnostische hartkatheterisatie of percutane cardiale interventieprocedure ondergingen, uitgevoerd met een 7F-huls.                                                                                                                                     | Indicatie: diagnostische of invasieve hartkatheterisatie via de arteria femoralis<br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yr)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yr) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | <ul style="list-style-type: none"><li>met of zonder slijpeling, maar zonder extra compressie, handmatig of mechanisch.</li><li>Veiligheidseindpunt: incidentie van bijwerkingen – kleine en grote vasculaire complicaties en alle andere bijwerkingen – ernstig en niet-ernstig tijdens de duur van het onderzoek (d.w.z. tot ontslag van de patiënt).</li></ul> <p>Uitkomsten</p> <ul style="list-style-type: none"><li>Gemiddelde tijd tot hemostase</li><li>Diagnose: 56,6 ± 29 seconden</li><li>Interventioneel 59,9 ± 16,2 seconden</li><li>Alle patiënten 57,8 ±26,3</li><li>Alle patiënten waren na 4 uur bedrust ambulante zonder problemen.</li></ul> <p>Veiligheidsresultaten</p> <ul style="list-style-type: none"><li>49/50 (98%) vrij van vasculaire complicaties tot ontslag uit het ziekenhuis</li><li>Gemiddelde tijd tot ontslag 2,6 dagen</li><li>1/50 (2%) lichte bloeding de volgende dag na probleemloze ambulante op de dag van de angiografie</li></ul> |
| n                                                                              | 50                                 |                       |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| men                                                                            | 35 (70%)                           |                       |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| women                                                                          | 15 (30%)                           |                       |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| PCI cases                                                                      | 15                                 |                       |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| age (yr)                                                                       | 62.8±11.1                          |                       |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| body mass index (kg/m²)                                                        | 25.4±6.7                           |                       |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| systolic BP (mmHg)                                                             | 131.2±20.9                         |                       |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| diastolic BP (mmHg)                                                            | 77.9±10.6                          |                       |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| diabetes mellitus                                                              | 9 (18%)                            |                       |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| arterial hypertension                                                          | 34 (68%)                           |                       |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| previous coronary intervention                                                 | 13 (26%)                           |                       |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| preprocedure aspirin                                                           | 50 (100%)                          |                       |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| preprocedure clopidogrel                                                       | 50 (100%)                          |                       |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Procedural unfractionated heparin                                              | 15 (30%)                           |                       |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Procedural abciximab                                                           | 2 (4%)                             |                       |                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009) | 2009 RADI                          | Post-market onderzoek | <p>Het onderzoek is bedoeld om te informeren als klanten/gebruikers problemen met de nieuwe verpakking ervaren, met name de niet-steriele buitenkant van het Tuvek/PET-PE-zakje.</p> <p>Het onderzoek dient ook informatie te geven over het feit of de behandelend arts verschillen waarneemt in de toepassings-/plaatsingsstappen van het</p> | 25 apparaten<br>4 Zweedse ziekenhuizen<br><br>16/25 (64%) van de patiënten waren PCI-patiënten met zware anticoagulatiemedicatie                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | <p>Uitkomsten</p> <ol style="list-style-type: none"><li>Verpakkingsgerelateerde problemen – 21/25 (84%) toepassingen waren succesvol; 4/25 (16%) waren niet succesvol (1 – testen van nieuwe introducer, 1 binnenschijf ging door de arteriotomie bij de stap van de backing, de knop kwam omhoog en buitenste schijf werd geplaatst in het incisieweefselkanaal, 2 onmiddellijke hemostase werd niet bereikt ondanks de afwezigheid van implementatieproblemen.)</li></ol> |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

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|----------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                        |                                                     |                                                                  | <p>apparaat in vergelijking met eerder gebruikte apparaten.</p> <p>Het onderzoek moet ook input geven over eventuele verdere behoeften aan verbetering van de productkwaliteit.</p>                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | <p>2. Onmiddellijke hemostase 19/25 (76%) patiënten</p> <p>3. Bloeding 11/25 (44%) - 9/25 (36%)<br/>sijpelen/bloeding, 2/25 (8%) hematomen</p> <p>Totaal gebeurtenispercentage 19%</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <p>The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022)</p> | <p>2022/<br/>Terumo<br/>Medical<br/>Corporation</p> | <p>Prospectief, multi-centrisch, observationeel, post-market</p> | <p>Het doel van dit onderzoek is om de veiligheid en effectiviteit van FemoSeal™ VCS verder aan te tonen bij het bereiken van hemostase op toegangslocaties in de arteria femoralis (CFA) bij patiënten uit de praktijk die percutane endovasculaire procedures ondergaan</p> | <ul style="list-style-type: none"> <li>• Patiëntenopvolging na 30 dagen (<math>\pm 7</math> dagen) door ziekenhuisbezoek of telefonische oproep.</li> <li>• Registratie: december 2021 tot juli 2022.</li> <li>• 230 ingeschreven proefpersonen die diagnostische of interventionele endovasculaire procedures ondergaan waarbij FemoSeal™ wordt gebruikt.</li> </ul> <p>3 Europese locaties: Frankrijk (92 patiënten), Duitsland (38 patiënten), België (100 patiënten).</p> | <ul style="list-style-type: none"> <li>• <b>Demografie/comorbiditeit en:</b> <ul style="list-style-type: none"> <li>- Geslacht: 161 mannen (70%)/69 vrouwen (30%).</li> <li>- Gemiddelde leeftijd: <math>70 \pm 12</math>.</li> <li>- BMI: <math>26,1 \pm 4,95</math> kg/m<sup>2</sup>.</li> <li>- Hypertensie: 160 patiënten (69,6%).</li> <li>- Dyslipidemie: 128 (55,7%).</li> <li>- Coronaire hartziekte: 42 (18,3%).</li> <li>- Rookt op dit moment: 86 (37,6%).</li> <li>- Heeft in het verleden gerookt: 66 (28,8%).</li> <li>- Coronaire hartziekte: 34 (14%).</li> <li>- Eerder myocardinfarct: 18 (7,8%).</li> <li>- Perifere arteriële revascularisatie: 12 (5,2%) in de halsslagader en 83 (37,5%) in de ader van de onderste ledematen.</li> <li>- Antibloedplaatjestherapie (bij baseline): 211 (91,7%), waaronder 21 (9,1%) dubbele antibloedplaatjestherapie (DAPT).</li> <li>- Antistolling oraal: 40 (17,4%) patiënten.</li> </ul> </li> <li>• <b>Interventiekenmerken:</b> <ul style="list-style-type: none"> <li>- Instelling: ziekenhuis 162 gevallen (70,4%), polikliniek 68 gevallen (29,6%).</li> <li>- Dominante indicatie: claudication 147 gevallen (63,9%).</li> </ul> </li> </ul> |

|  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
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|  |  |  |  |  | <ul style="list-style-type: none"> <li>- Benadering: 35 antegrade (15,3%), 194 retrograde (84,7%).</li> <li>• <b>Primaire eindpunten:</b> <ul style="list-style-type: none"> <li>- Gecombineerd eindpunt veiligheid (geen ernstige complicaties in de ledemaat van de toegangsplaats binnen 6 uur na de procedure) en doeltreffendheid (succesvolle hemostase van het aanprikpunt) behaald in 215 van de 226 gevallen (95,1%) [95% CI: 91,46; 97,55] patiënten in de volledige analyseset en 215/230 (93,5%) [95% CI 89,47, 96,30] in de met FemoSeal™ behandelde set.</li> <li>- Het effectiviteitseindpunt werd bereikt bij 219/226 (96,9%) CI [93,7, 98,7] patiënten.</li> <li>- Veiligheidseindpunt bereikt bij 220/230 (95,2%) [95% CI: 92,15, 97,90] patiënten.</li> </ul> </li> <li>• <b>Secundaire eindpunten:</b> <ul style="list-style-type: none"> <li>- Geen kleine complicaties op de toegangsplaats gedurende zes uur na de procedure bereikt bij 225 van de 230 gevallen (97,8%) [95% CI: 95,00; 99,29].</li> <li>- Bij 219/230 (95,2%) [95% CI:91,60; 97,59] patiënten werden zes uur tot 30 dagen na de ingreep geen ernstige of lichte complicaties bij de toegangsplaats waargenomen.</li> <li>- Gemiddelde tijd tot hemostase met FemoSeal™ VCD: 0,42 (0,25; 0,50) minuten.</li> <li>- Gemiddelde tijd tot ambulantie: 5,00 (4,54; 5,50) minuten.</li> </ul> </li> </ul> |
|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|--|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <ul style="list-style-type: none"> <li>- Gemiddelde verblijfsduur in het ziekenhuis: 23,98 uur (22,72 uur, 25 uur).</li> <li>- Bruikbaarheid van FemoSeal™ VCS: 'gemakkelijk' of 'zeer gemakkelijk' te plaatsen in 98,7% van de gevallen ('gemakkelijk' te plaatsen in 21 (9,2%), 'zeer gemakkelijk' te plaatsen in 205 (89,5%)) met geen of lage weerstand bij het plaatsen bij 226 (98,3%) van de gevallen.</li> </ul> <p>152 (66,1%) van de 230 patiënten die werden behandeld met de voerdraad die bij de FemoSeal™-kit (GW 0,038") is geleverd en voor de FemoSeal™ wordt aanbevolen, hebben geen gebreken aan het apparaat of bijwerkingen gemeld.</p> |
|--|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Het onderzoek uit 2006 werd uitgevoerd om de veiligheid en effectiviteit van het huidige hulpmiddel te bevestigen met een verbeterd toedieningssysteem en om feedback te krijgen over de gebruiksaanwijzing van FemoSeal™ VCS en het trainingsprogramma. Het onderzoek omvatte 100 patiënten en het primaire eindpunt was of hemostase werd bereikt of dat aanvullende handmatige of mechanische compressies nodig waren. Uit dit onderzoek is gebleken dat de toepassing van FemoSeal™ VCS in de meeste gevallen succesvol was (91% bereikte onmiddellijke hemostase).

In het onderzoek van 2008 waren er 50 deelnemers om de veiligheid en prestaties van FemoSeal™ VCS te beoordelen bij gebruik tijdens een normale klinische routine bij patiënten die een cardiale katheterisatie met een huls van 7 Fr ondergaan. Het primaire eindpunt voor het onderzoek was het verzamelen van gegevens over de tijd tot hemostase en de tijd tot ambulante zonder extra compressie, handmatig of mechanisch. De onderzoeksresultaten concludeerden dat de gemiddelde tijd tot hemostase 57,8 seconden was en dat alle patiënten na 4 uur bedrust ambulant waren.

De studie van 2009 was bedoeld om de nieuwe FemoSeal™ VCS-verpakking te evalueren. Er namen 25 patiënten deel aan het onderzoek. Het primaire eindpunt was of de gebruiker problemen had met de verpakking. De gebruikers gaven aan geen problemen te hebben met de nieuwe FemoSeal™ VCS-verpakking. Dit onderzoek verzamelde ook gegevens voor de tijd tot hemostase.

Het doel van het onderzoek uit 2022 is om de veiligheid en effectiviteit van FemoSeal VCS verder aan te tonen bij het bereiken van hemostase op toegangslocaties in de arteria femoralis (CFA) bij patiënten uit de praktijk die percutane endovasculaire procedures ondergaan. Aan dit onderzoek namen 230 patiënten deel. Primaire eindpunten voor de registratie zijn het slagen van de procedure (d.w.z. succesvolle hemostase van de punctieplaats) en het verminderen van ernstige complicaties (bijv. vasculair letsel, bloedingen gerelateerd aan de toegangsplaats, infectie van de toegangsplaats, herhaalde handmatige compressie en nieuwe ipsilaterale acute beenischemie gerelateerd aan de toegangsplaats). Het onderzoek concludeerde dat de FemoSeal™ VCS goed presteert in reële omgevingen en effectieve hemostase en lage percentages complicaties op de toegangsplaats biedt voor patiënten die perifere endovasculaire interventies ondergaan. Het apparaat heeft goede prestaties met een korte tijd tot hemostase en goede gebruikersfeedback, waardoor FemoSeal™ VCS een waardevol apparaat is voor femorale toegangssluiting.

### 1.4.3 Samenvatting van gegevens uit klinische post-market onderzoeken

#### 1.4.3.1 Voltooide post-market klinische follow up

Een samenvatting van de voltooide klinische post-market follow-upactiviteiten wordt beschreven in **Tabel 1.7** hieronder.

**Tabel 1.7. Klinische post-market follow-upactiviteiten**

| Voltooide klinische post-market follow-upactiviteiten                     |          |                                                               |                                                                                                                                                                                                    |                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|---------------------------------------------------------------------------|----------|---------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Naam activiteit                                                           | Jaar/ CI | Type onderzoek                                                | Doelen                                                                                                                                                                                             | Mijlpalen                                                                                                                                           | Criteria voor potentiële acceptatie                                                                                                                                                                                                                                                                                                                                                                                                           |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021 TMC | Klinisch post-market onderzoek – onderzoek van hoge kwaliteit | Post-market onderzoek om prospectieve feedback te verzamelen met betrekking tot het gebruik van het FemoSeal™ Vascular Closure System dat op de markten van de Europese Unie wordt gedistribueerd. | <ul style="list-style-type: none"> <li>120 gevallen</li> <li>8 unieke artsen met &gt; 5 jaar ervaring</li> <li>Meerdere landen in Europa</li> </ul> | <p><b>Evaluatie hulpmiddel op schaal van 1 tot 5 – Stellingen in enquête</b></p> <ul style="list-style-type: none"> <li>Acceptatiecriteria <ul style="list-style-type: none"> <li>Resultaten 3-5 worden als positief beschouwd</li> <li>Alle uitspraken moeten <math>\geq 80\%</math> positieve feedback hebben</li> </ul> </li> <li>Uitkomsten <ul style="list-style-type: none"> <li>Geen enkele stelling kreeg &gt;</li> </ul> </li> </ul> |



| Voltooide klinische post-market follow-upactiviteiten                          |                  |                                                               |                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|--------------------------------------------------------------------------------|------------------|---------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                |                  |                                                               |                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                      | <p>20% negatieve feedback</p> <ul style="list-style-type: none"> <li>Er zijn geen klachten over het product gemeld</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                    |
| 20210298 – 0.035” and 0038” Guidewire Clinical Survey Report (2021)            | 2021 TMC         | Klinisch post-market onderzoek – onderzoek van hoge kwaliteit | Post-market onderzoek om prospectieve feedback te verzamelen met betrekking tot het gebruik van de voerdraad van 0,035” meegeleverd met het 6Fr Angio-Seal™ VIP Vascular Closure Device (VCD) en de voerdraad van 0,038” meegeleverd met zowel het 8Fr Angio-Seal™ VIP VCD als het FemoSeal Vascular Closure System die in de Europese Unie worden gedistribueerd. | <ul style="list-style-type: none"> <li>Onderzoeken betreffende de 0,035” draad <ul style="list-style-type: none"> <li>106 enquêtes</li> <li>64 artsen</li> </ul> </li> <li>Onderzoeken betreffende de 0,038” draad <ul style="list-style-type: none"> <li>109 enquêtes</li> <li>55 artsen</li> </ul> </li> <li>12 retrospectieve enquêtes</li> </ul> | <p><b>Evaluatie hulpmiddel op schaal van 1 tot 5 – Stellingen in enquête</b></p> <ul style="list-style-type: none"> <li>Acceptatiecriteria <ul style="list-style-type: none"> <li>Resultaten 3-5 worden als positief beschouwd</li> <li>Alle uitspraken moeten <math>\geq 80\%</math> positieve feedback hebben</li> </ul> </li> <li>Uitkomsten <ul style="list-style-type: none"> <li>Alle voerdraden kregen aanvaardbare ratings</li> <li>Er zijn geen klachten over het product gemeld</li> </ul> </li> </ul> |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps | 2023-2024 TMC/TE | Klinisch post-market onderzoek – onderzoek van hoge kwaliteit | Prospectief feedback verzamelen met betrekking tot het gebruik van FemoSeal VCS met voerdraden die op de EU-                                                                                                                                                                                                                                                       | <ul style="list-style-type: none"> <li>126 enquêtes <ul style="list-style-type: none"> <li>7 locaties</li> <li>5 landen</li> </ul> </li> <li>14 november 2023 – 11 juni 2024</li> <li>Medisch specialisme arts: <ul style="list-style-type: none"> <li>Vaatchirurgie</li> </ul> </li> </ul>                                                          | <p><b>Evaluatie hulpmiddel op schaal van 1 tot 5 – Stellingen in enquête</b></p> <ul style="list-style-type: none"> <li>Acceptatiecriteria <ul style="list-style-type: none"> <li>Resultaten 3-5 worden als positief beschouwd</li> <li>Alle uitspraken moeten <math>\geq 80\%</math></li> </ul> </li> </ul>                                                                                                                                                                                                     |

| Voltooide klinische post-market follow-upactiviteiten |  |  |                              |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|-------------------------------------------------------|--|--|------------------------------|--------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Identified in CER-FS-2021 and CER-FS-2022 (2023)      |  |  | markt worden gedistribueerd. | <ul style="list-style-type: none"> <li>○ Interventie-radiologie</li> <li>○ Angiologie</li> </ul> | <p>positieve feedback hebben</p> <ul style="list-style-type: none"> <li>○ Als er zich bij dit onderzoek ongewenste voorvallen voordoen, moeten deze door het risicobeheer worden verwacht.</li> </ul> <ul style="list-style-type: none"> <li>• Demografische gegevens patiënt <ul style="list-style-type: none"> <li>○ Vrouw: 29,4% (37/126)</li> <li>○ Man: 69,8% (88/126)</li> <li>○ Geslacht niet bekendgemaakt : 0,8 (1/126)</li> <li>○ Leeftijd &gt;75 jaar: 31,7%</li> </ul> </li> <li>• Uitkomsten <ul style="list-style-type: none"> <li>○ Voedraad meegeleverd met FemoSeal™ VCS: 101/126 (80,2%).</li> <li>○ Maximale proceduretijd (minuten): 63,4 (36,6) (gemiddelde (SD)); 57,0 (36,0-81,0) (mediaan (IQR))</li> <li>○ Alle prestatiebeoordelingen van FemoSeal™ VCS waren gunstig.</li> <li>○ Alle beoordelingen</li> </ul> </li> </ul> |

| Voltooide klinische post-market follow-upactiviteiten |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                           |
|-------------------------------------------------------|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                       |  |  |  |  | <p>voor geleverde FemoSeal™ VCS voerdraad waren gunstig.</p> <ul style="list-style-type: none"> <li>o Eén ongewenst voorval (0,8%): de FemoSeal™ VCS-schijven waren waarschijnlijk niet goed uitgelijnd vanwege het gebruik van een stijve voerdraad (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035") waardoor handmatige compressie nodig was om hemostase te bereiken.</li> </ul> |

Terumo Medical Corporation heeft drie hoogwaardige gebruikersenquêtes onder artsen uitgevoerd tijdens de huidige rapportageperiode (1 september 2019 – 31 augustus 2024).

De FemoSeal™ klinische enquêtes verzamelden proactieve klinische gegevens met betrekking tot de veiligheid en prestaties van FemoSeal™ VCS tijdens klinisch gebruik. Het onderzoek omvatte vragen over het gehele apparaat en de bijbehorende accessoires, waaronder de 0,038" voerdraad en de directe interacties daarvan. De klinische enquêtes over de voerdraad verzamelden proactieve klinische gegevens met betrekking tot veiligheid en prestaties tijdens klinisch gebruik van de 0,038" voerdraad die bij FemoSeal™ VCS wordt geleverd. De vragen waren specifiek gericht op het algemene gebruik van de voerdraad, variërend van het inbrengen via de procedureschacht in het vaatstelsel tot het verwijderen van de draad.

FemoSeal™ VCS en de 0,038" voerdraad die bij het hulpmiddel wordt geleverd, ontvingen alle aanvaardbare beoordelingen en er werden zes (6) klachten ingediend over het hulpmiddel en negen (9) meldingen over de voerdraad op basis van de evaluatie van de opmerkingen die uit de hoogwaardige klinische enquêtes verkregen werd. De klachten zijn beoordeeld voor zowel de

FemoSeal als de voerdraad en zijn beoordeeld als onderdeel van het Terumo-proces voor post-market toezicht. Er werden geen nieuwe risico's en/of risiconiveaus vastgesteld.

In het kader van de PMCF-activiteiten werd in 2024 een gebruikersenquête voor artsen afgerond. De resultaten van het onderzoek toonden aan dat de prestatiebeoordeling en veiligheid van FemoSeal™ VCS over het algemeen zeer gunstig waren. De compatibiliteit van andere voerdraaden dan die standaard bij de FemoSeal™ VCS wordt geleverd, werd ook aangetoond.

#### **1.4.3.2 Voortdurende of geplande post-market klinische follow-up**

TMC heeft twee lopende/geplande post-market klinische follow-upactiviteiten. Daarnaast zal een klinische enquête worden uitgevoerd om toekomstige feedback te verzamelen met betrekking tot het gebruik van de voerdraad die bij FemoSeal VCS wordt geleverd op de EU-markt. De enquête wordt ingevuld door artsen om te onderzoeken welke voerdraaden zij tijdens de procedure hebben gebruikt. Het doel van deze enquête is om een lacune te onderzoeken die is geïdentificeerd als een gebrek aan literatuur en commentaar van externe beoordelaars over de compatibiliteit van FemoSeal™ VCS met voerdraaden van andere merken dan Terumo. De feedback omvat technische resultaten, klinische prestaties en veiligheid met betrekking tot de prestaties van het apparaat met verschillende voerdraaden.

#### **1.4.4 Samenvatting van gegevens uit systematisch literatuuronderzoek**

Terumo Medical Corporation voert systematisch literatuurstudies uit om klinische veiligheids- en prestatiegegevens van gepubliceerde onderzoeken naar FemoSeal™ VCS en/of soortgelijke apparaten te verzamelen en te evalueren. Het doel van de jaarlijkse screening van de gepubliceerde literatuur is het identificeren van eerder onbekende bijwerkingen, het monitoren van bekende bijwerkingen, het identificeren van opkomende risico's en het identificeren van mogelijk systematisch misbruik of off-label gebruik van FemoSeal™ VCS.

In de meest recente systematische literatuurstudie, die betrekking had op de periode van 1 september 2019 tot en met 31 augustus 2024, werden 29 gepubliceerde studies geïdentificeerd die klinische veiligheids- en prestatiegegevens leverden over FemoSeal™ VCS. 23 referenties rapporteerden on-labelgebruik van FemoSeal™ VCS en off-labelgebruik werd gemeld in 9 gevallen. Over het algemeen toont de literatuur over studies die specifiek zijn voor het gebruik van FemoSeal™ VCS zijn gebruikt, een populatie in onderzoek die representatief is voor patiënten in de EU die percutane vasculaire katheterisatieprocedures ondergaan. Zie **sectie 3** voor een lijst van deze 23 on-label peer-reviewed publicaties.

De klinische prestaties werden beoordeeld aan de hand van de volgende maatregelen:

- De tijd tot hemostase is korter dan of vergelijkbaar met de 'state of the art' voor percutane sluiting van de dijslagader.

- Tijd tot ambulantie is korter dan of vergelijkbaar met de 'state of the art' voor percutane sluiting van de dijslagader.
- Het percentage postoperatieve complicaties is vergelijkbaar met of lager dan de huidige zorgstandaarden.

Op basis van deze klinische prestatiemetingen toonden de gegevens in deze literatuurstudie aan dat FemoSeal™ VCS met succes kan worden gebruikt bij het sluiten van de femorale arteriële punctie (arteriotomie) bij patiënten die percutane katheterisatie hebben ondergaan met een 7 Fr of smallere procedureschacht. Volledige hemostase werd bereikt bij de meerderheid van de patiënten (79,65-100%) en werd geassocieerd met een mediane tijd tot hemostase van 0,5 min, gemiddelde tijd tot ontslag van 3 dagen. Tussen 69,2 en 86,7% van de patiënten was na 5 uur in staat op te staan, met een gemiddelde postoperatieve bedtijd van 349 min. FemoSeal™ VCS-falen werd waargenomen in 3,68-4% van de gevallen en bij 0,9-4,4% van de ingrepen was extra handmatige compressie nodig.

De klinische veiligheid werd beoordeeld aan de hand van bijwerkingen, met inbegrip van, maar niet beperkt tot:

- Bloeding
- Hematoom
- Pseudoaneurysma
- Blauwe plekken
- Arterioveneuze fistel
- Infectie
- Overlijden

Voor elk van deze ongewenste voorvallen was de voor FemoSeal™ VCS gemelde frequentie van voorvallen in de opgenomen onderzoeken lager dan of vergelijkbaar met de historisch gemelde frequenties voor handmatige compressie en andere vasculaire sluitinstrumenten.

Er werden geen ongewenste voorvallen vastgesteld bij de beoordeling van 10 procedurerapporten, aangezien er geen nieuwe, onverwachte, opkomende of onaanvaardbare risico's werden vastgesteld.

De algehele effectiviteit van het gebruik van FemoSeal™ VCS tijdens diagnostische angiografie of interventionele operaties hangt af van meerdere factoren, zoals: geslacht, leeftijd, anatomie van de patiënt, comorbiditeiten, anatomische plaatsing van het aanprikpunt, ervaring van de chirurg, plaatsingsmethode van de VCD, postoperatieve zorg, enz. Naast technisch succes, waaronder het bereiken van hemostase, bood FemoSeal™ VCS klinische voordelen met betrekking tot vasculaire sluiting na femorale arteriële punctie, zoals een verkorting van de tijd tot hemostase en een verkorting van de tijd tot ambulantie. De prestatieresultaten van FemoSeal™ VCS komen overeen

met de resultaten die worden verwacht voor dit type apparaat bij beoogd gebruik. Een aantal referenties dat tijdens de huidige zoekperiode werd opgehaald, toonde het gebruik van het onderzoeksinstrument op een andere anatomische locatie dan de dijbeenslagader en voor het sluiten van arteriotomieën > 7 Fr, wat als off-label wordt beschouwd.

Tijdens de beoordeling werden geen onbekende bijwerkingen, opkomende risico's of mogelijk systematisch misbruik van het hulpmiddel vastgesteld. Als het FemoSeal™ VCS echter met zorg wordt gebruikt door getrainde artsen, functioneert het medisch hulpmiddel als een nuttig en noodzakelijk klinisch hulpmiddel. Over het algemeen beantwoordt de doeltherapie en dus FemoSeal™ VCS aan de klinische behoefte die momenteel bestaat bij de behandeling van complicaties in verband met vasculaire toegang.

In het algemeen werden in de gegevens in deze literatuurstudie geen prestatie- of veiligheidsproblemen vastgesteld in de klinische omgeving die eerder niet bekend waren, of schadelijke effecten die zich bij hogere dan verwachte/aanvaardbare percentages voordeden. Daarom kan uit deze literatuurstudie worden geconcludeerd dat FemoSeal™ VCS, indien gebruikt om compressie voor hemostase bij een arteriotomie na percutane katheterisatie te bereiken, naar verwachting blijft werken en niet in verband wordt gebracht met ernstige veiligheidsgebeurtenissen.

#### **1.4.5 Samenvatting van gegevens uit klinische post-market onderzoeken**

Er is een proactief PMS-systeem aanwezig en alle klachten worden maandelijks beoordeeld in overeenstemming met de interne productieprocedures. De klachtgegevens zijn geanalyseerd in de periode van 1 september 2019 tot 31 augustus 2024. In totaal kwamen er 28 Medical Device Vigilance (MDV) Reports en 476 klachtenmeldingen van klanten binnen bij de fabrikant. Van de 28 MDV-rapporten hadden er 27 betrekking op bijwerkingen en één op een storing van het hulpmiddel. Er vonden twee sterfgevallen plaats tijdens de rapportageperiode, maar geen van de gerapporteerde sterfgevallen werd geacht gerelateerd te zijn aan het hulpmiddel. Van de 476 klachten bij de fabrikant waren de meest voorkomende redenen voor de klachten moeilijkheden bij het inbrengen (146 gevallen, 0,0142% incidentiepercentage). De uitvalmodus van pull-outgebeurtenissen is de op één na meest voorkomende met een percentage van 0,0126% (130 gebeurtenissen).

Het FemoSeal™ Vascular Closure System is wereldwijd meer dan 1.030.136 keer verkocht, waarvan 827.843 keer in de Europese Economische Ruimte. De berekende frequentie van klachten op basis van wereldwijde verkoop is 0,046%. Het totale aantal klachten van klanten is zeer laag. Er zijn geen nieuwe risico's geïdentificeerd die niet in de gebruiksaanwijzing en de risicodocumentatie zijn opgenomen.

De frequentie waarmee ongewenste bijwerkingen optreden, wordt weergegeven in **Tabel 1.2**. Er werden door de klachten geen nieuwe onverwachte, opkomende of onaanvaardbare risico's geïdentificeerd. Er waren geen significante toenames in de frequentie of ernst van bekende bijwerkingen.

#### **1.4.6 Algemene samenvatting van klinische prestaties en veiligheid**

FemoSeal™ VCS is geïndiceerd voor gebruik bij het sluiten van de beenslagaderpunctie (arteriotomie) bij patiënten die percutane katheterisatie hebben ondergaan met een 7F (2,33 mm) of kleinere procedurehuls. Deze klinische evaluatie is gebaseerd op een uitgebreide analyse van beschikbare pre- en post-market klinische gegevens en literatuur die relevant zijn voor het beoogde gebruik van FemoSeal™ VCS.

Er is een uitgebreide beoordeling van de gepubliceerde literatuur uitgevoerd voor de periode van 1 september 2019 tot en met 31 augustus 2024. Het bewijsmateriaal omvatte 29 studies voor FemoSeal™ VCS. Het bewijsmateriaal dat in de klinische evaluatie wordt geleverd, concludeert dat het onderzochte apparaat veilig en effectief is wanneer het wordt gebruikt zoals aangegeven en dat alle risico's of ongewenste bijwerkingen die onder normale gebruiksomstandigheden met het apparaat kunnen worden geassocieerd, aanvaardbare risico's vormen wanneer ze worden afgewogen tegen de voordelen voor de patiënt. De prestatieresultaten van de betrokken apparaten komen overeen met de resultaten die worden verwacht voor dit type apparaat bij beoogd gebruik.

De mogelijke ongewenste bijwerkingen die verband houden met het gebruik van FemoSeal™ VCS omvatten de bijwerkingen die ook vaak worden gemeld met alternatieve manieren van sluiting van de arteriotomie, zoals bloeding en hematoom. Over het algemeen zijn de incidentiecijfers voor de bijwerkingen die worden gemeld met het gebruik van FemoSeal™ VCS vergelijkbaar met de cijfers die worden gemeld naar aanleiding van handmatige compressie en vergelijkbare vasculaire sluitinstrumenten. Specifiek, voor bloedingen en hematoom, zijn de gerapporteerde percentages voor FemoSeal™ VCS lager dan de gerapporteerde percentages voor vergelijkbare vasculaire sluitinstrumenten. Elk van de gemelde ongewenste voorvallen, zowel uit de gepubliceerde literatuur als uit het post-market toezicht, was reeds eerder geïdentificeerd (zie **Section 1.3**).

De bestaande gegevens met betrekking tot de klinische veiligheid en prestaties van FemoSeal VCS suggereren dat de voordelen van het gebruik van dit vasculaire sluitinstrument voor de patiënt zwaarder wegen dan mogelijke risico's wanneer het wordt gebruikt in overeenstemming met de gebruiksaanwijzing.

Zoals aangegeven in de voorgaande paragrafen, tonen de gegevens die worden verstrekt voor FemoSeal™ VCS de consistentie aan tussen de gegevens met betrekking tot het te evalueren hulpmiddel (bijv. gebruik van het hulpmiddel, veiligheidsresultaten, klinische prestaties en klinische voordelen), geïdentificeerde gelijkwaardige hulpmiddelen en de gegevens met betrekking tot vergelijkbare hulpmiddelen conform de 'state of the art'.

Uit de kruisanalyse van veiligheidsgegevens zijn geen hiaten gebleken tussen:

- Gegevens conform de state of the art
- Specifieke gegevens van het te evalueren hulpmiddel



- Gegevens vermeld in risicobeheerdossier(s)
- Gegevens vermeld in de etikettering en/of gebruiksaanwijzing (d.w.z. restrisiko's die aan de gebruiker moeten worden gemeld).

Klinische veiligheid is aangetoond door lage aantallen complicaties die zijn geïdentificeerd in de gepubliceerde peer-reviewed klinische literatuur, door het bedrijf gesponsorde klinische studies, beoordeling van de post-market gegevens in combinatie met geen terugtrekkingen uit de markt. Er zijn geen problemen met de prestaties vastgesteld. De literatuur bevatte het gebruik van FemoSeal™ VCS dat overeenstemde met het beoogde gebruik van de fabrikant.

### **1.5 Mogelijke diagnostische of therapeutische alternatieven**

Handmatige compressie wordt traditioneel gebruikt om hemostase te bereiken op de arteriotomieplaats na vasculaire katheterisatie. Handmatige compressie wordt in verband gebracht met langdurige immobilisatie van de patiënt (tot 8 uur na een ingreep) en met aanzienlijk ongemak en langdurig ziekenhuisverblijf. Uit een recente systematische evaluatie bleek dat de mediane tijd om hemostase te bereiken met handmatige compressie 20,8 minuten was.<sup>1</sup>

Alternatieven voor handmatige compressie zijn onder meer externe hemostatische apparaten die mechanische compressie toepassen op de arteriotomieplaats. Deze apparaten verkorten de tijd tot hemostase of de tijd tot ambulante niet, maar verlagen de personeelsbehoefte door handmatige compressie te vervangen door mechanische compressie. De frequentie van bijwerkingen die verband houden met het gebruik van mechanische compressie is vergelijkbaar met die van handmatige compressie.

Vasculaire sluitinstrumenten, zoals FemoSeal™ VCS, zijn ontworpen om de arteriotomie te sluiten. Ze zijn bedoeld om de tijd tot hemostase te verkorten en eerdere ambulante mogelijk te maken. Uit een recente systematische evaluatie met 13 in de handel verkrijgbare hulpmiddelen, bleek dat de mediane tijd om hemostase te bereiken 5,4 minuten was met een vasculair sluitinstrument. De mediane hemostasetijd van het afzonderlijke vasculaire sluitinstrument varieerde van 1 minuut (FemoSeal™ VCS) tot 14 minuten; het merendeel van de instrumenten zat tussen 4 en 10 minuten.<sup>1</sup>

Vaak gemelde bijwerkingen in verband met sluiting van de arteriotomieplaats, met handmatige compressie, externe hemostatische apparaten of vasculaire sluitinstrumenten, zijn onder meer hematoom, bloeding op de toegangsplaats, pseudo-aneurysma, arterioveneuze fistel en infectie. Uit dezelfde systematische evaluatie (34 gerandomiseerde gecontroleerde onderzoeken, 14.401 patiënten) bleek dat het aantal ongewenste voorvallen vergelijkbaar was tussen handmatige compressie en het gebruik van vasculaire sluitinstrumenten, met de uitzondering dat bloedingen doorgaans iets vaker voorkwamen bij vasculaire sluitinstrumenten.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure*



*Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Voorgesteld gebruikersprofiel en training

De beoogde gebruikers van het FemoSeal™ Vascular Closure System zijn artsen met een opleiding die hen in staat stelt arteriële toegang en sluiting uit te voeren voor endovasculaire procedures via de beenslagader en die hebben deelgenomen aan een instructieprogramma voor artsen van Terumo Medical Corporation FemoSeal™.

## 1.7 Relevante geharmoniseerde en gemeenschappelijke normen

| Standaardreferentie | Huidig jaar conformiteit/rev | Beschrijving                                                                                                                             |
|---------------------|------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070           | 2014/AMD1:2018               | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070        | 2014/A1:2018                 | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance        | 20 mei 2021                  | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052          | 2015                         | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213          | 2017                         | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503          | 2020                         | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182          | 2019                         | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |
| EN ISO 13485        | 2016/A11:2021                | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 13485           | 2016                         | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |

| Standaardreferentie | Huidig jaar conformiteit/rev | Beschrijving                                                                                                                                                             |
|---------------------|------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14644-1         | 2015                         | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1      | 2015                         | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2         | 2015                         | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2      | 2015                         | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3         | 2019                         | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3      | 2019                         | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1         | 2003                         | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1      | 2003                         | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2         | 2003/TC1:2004                | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| EN ISO 14698-2      | 2003/TC 1:2004               | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| USP <788>           | N.v.t.                       | PARTICULATE MATTER IN INJECTIONS                                                                                                                                         |

| Standaardreferentie  | Huidig jaar conformiteit/rev | Beschrijving                                                                                                         |
|----------------------|------------------------------|----------------------------------------------------------------------------------------------------------------------|
| EU-farmacopee 2.9.19 | N.v.t.                       | Particulate Contamination: Sub-Visible Particles                                                                     |
| IEC 62366-1          | 2015                         | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN 62366-1           | 2015                         | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN ISO 14971         | 2019/A11:2021                | Medical devices — Application of risk management to Medical devices                                                  |
| ISO 14971            | 2019                         | Medical devices — Application of risk management to Medical devices                                                  |
| ASTM F1980           | 2016                         | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1       | 2020                         | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1          | 2018                         | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2       | 2006                         | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2          | 2006                         | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3       | 2014                         | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3          | 2014                         | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4       | 2017                         | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4          | 2017                         | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |

| Standaardreferentie | Huidig jaar conformiteit/rev | Beschrijving                                                                                                                               |
|---------------------|------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-5      | 2009                         | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                                         |
| ISO 10993-5         | 2009                         | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                                         |
| EN ISO 10993-6      | 2016                         | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| ISO 10993-6         | 2016                         | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| EN ISO 10993-10     | 2023                         | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| ISO 10993-10        | 2021                         | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| EN ISO 10993-11     | 2018                         | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| ISO 10993-11        | 2017                         | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| EN ISO 10993-12     | 2021                         | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| ISO 10993-12        | 2021                         | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| EN ISO 10993-17     | 2009                         | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17        | 2002                         | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18        | 2020/A1:2022                 | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |

| Standaardreferentie | Huidig jaar conformiteit/rev | Beschrijving                                                                                                                                                                 |
|---------------------|------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-18     | 2020/A1:2022                 | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-23     | 2021                         | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23        | 2021                         | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382          | 2018                         | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756           | 2017                         | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>            | N.v.t.                       | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>           | N.v.t.                       | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72      | 2019                         | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135        | 2014/A1:2019                 | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135           | 2014/A1:2018                 | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7      | 2008/A1:2022                 | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |

| Standaardreferentie | Huidig jaar conformiteit/rev | Beschrijving                                                                                                                                                    |
|---------------------|------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-7         | 2008/A1:2019                 | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                               |
| EN 556-1            | 2024                         | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices |
| EN ISO 11737-1      | 2018/A1:2021                 | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11737-1         | 2018/A1:2021                 | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| EN ISO 11138-1      | 2017                         | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-1         | 2017                         | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| EN ISO 11138-2      | 2017                         | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 11138-2         | 2017                         | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| EN ISO 15223-1      | 2016                         | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| ISO 15223-1         | 2016                         | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| EN 1041             | 2008/A1:2013                 | Information supplied by the manufacturer of medical devices                                                                                                     |
| EN ISO 11607-1      | 2020/A1:2023                 | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                         |

| Standaardreferentie | Huidig jaar conformiteit/rev | Beschrijving                                                                                                                                                               |
|---------------------|------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11607-1         | 2019/A1:2023                 | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| EN ISO 11607-2      | 2020/A1:2023                 | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ISO 11607-2         | 2019/A1:2023                 | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169          | 2016                         | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M   | 2016                         | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825          | 2018                         | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096          | 2011 (R 2019)                | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M       | 2015                         | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24        | 2021                         | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3         | 2020                         | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |
| MDCG 2020-8         | 2020                         | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                             |
| MDCG 2020-7         | 2020                         | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                          |

| Standaardreferentie | Huidig jaar conformiteit/rev | Beschrijving                                                                                                                                                                                                                                                  |
|---------------------|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-6         | 2020                         | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                                                                                                          |
| MDCG 2019-9 v1      | 2022                         | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                                                                                      |
| MDCG 2019-8 v2      | 2020                         | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15        | 2020                         | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11        | 2021                         | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19        | 2021                         | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4      | 2021                         | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2         | 2019                         | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1         | 2019                         | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7         | 2018                         | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6         | 2018                         | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |



| Standaardreferentie | Huidig jaar conformiteit/rev | Beschrijving                                                                                                                                                                                  |
|---------------------|------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2018-4         | 2018                         | MDCG 2018-4 Annex: UDI database<br>Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                               |
| MDCG 2018-3 v1      | 2020                         | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25        | 2021                         | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2,12-2 Rev 2 | 2012                         | Guidance document medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                        |

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### 3.0 REVISIEGESCHIEDENIS

| SSCP-revisienummer       | Uitgiftedatum   | Beschrijving van de wijziging                                              | Revisie gevalideerd door de aangemelde instantie                                                                                                                                                                                                                                                                                                                  |
|--------------------------|-----------------|----------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022             | 20 januari 2023 | Eerste uitgave, bij MDR CE-certificering                                   | <p><input checked="" type="checkbox"/> Ja</p> <p>Validatietaal: English</p> <p><input type="checkbox"/> Nee (alleen van toepassing op implanteerbare apparaten van klasse IIa of enkele IIb (MDR, artikel 52, lid 4, 2e alinea) waarvoor het SSCP nog niet door de aangemelde instantie is gevalideerd)</p> <p><input type="checkbox"/> Overig (specificeer):</p> |
| SSCP-FS-2023 – Revisie 1 | 15 maart 2024   | Bijgewerkt voor de periode van 1 januari 2019 tot en met 31 december 2023. | <p><input checked="" type="checkbox"/> Ja</p> <p>Validatietaal: English</p> <p><input type="checkbox"/> Nee (alleen van toepassing op implanteerbare apparaten van klasse IIa of enkele IIb (MDR, artikel 52, lid 4, 2e alinea) waarvan het SSCP nog niet door de aangemelde instantie is gevalideerd)</p> <p><input type="checkbox"/> Overig (specificeer):</p>  |
| SSCP-FS-2024 Revisie 1   |                 | Bijgewerkt van 1 september 2019 tot en met 31 augustus 2024.               | <p><input type="checkbox"/> Ja</p> <p>Validatietaal: English</p> <p><input type="checkbox"/> Nee (alleen van toepassing op implanteerbare apparaten van klasse IIa of enkele IIb (MDR, artikel 52, lid 4, 2e alinea) waarvan het SSCP nog niet door de aangemelde instantie is gevalideerd)</p> <p><input type="checkbox"/> Overig (specificeer):</p>             |

|                           |               |                                                           |                                                                                                                                                                                                                                                                                                                                                                                                          |
|---------------------------|---------------|-----------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>Revisie 2 | June 20, 2025 | Herzien op basis van<br>vragen van NSAI voor<br>validatie | <div><input checked="" type="checkbox"/> Ja</div> <div>Validatietaal: English</div> <div><input type="checkbox"/> Nee (alleen van toepassing<br/>op implanteerbare apparaten<br/>van klasse IIa of enkele IIb<br/>(MDR, artikel 52, lid 4, 2e<br/>alinea) waarvan het SSCP nog<br/>niet door de aangemelde<br/>instantie is gevalideerd)</div> <div><input type="checkbox"/> Overig (specificeer):</div> |
|---------------------------|---------------|-----------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

## Oppsummering av sikkerhet og klinisk ytelse

### FemoSeal™ Vascular Closure System

|                                            |                                                                                             |
|--------------------------------------------|---------------------------------------------------------------------------------------------|
| <b>Produsent</b>                           | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 USA         |
| <b>Produsentens SRN</b>                    | US-MF-000019594                                                                             |
| <b>Ledelsens representant/PRRC</b>         | Kimberly Feitl<br>Vice President, Quality                                                   |
| <b>Basic UDI-DI</b>                        | 38970FS79                                                                                   |
| <b>EMDN-nummer</b>                         | C900199 – Hemostasesystemer-Annet                                                           |
| <b>Utstyrsklasse</b>                       | Klasse III                                                                                  |
| <b>Året da enheten først ble CE-merket</b> | 2005                                                                                        |
| <b>EU-representant</b>                     | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgia<br>SRN: BE-AR-000001433 |
| <b>Teknisk kontrollorgan</b>               | NSAI<br>CE 0050                                                                             |

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Denne oppsummeringen av sikkerhet og klinisk ytelse er ment å gi offentlig tilgang til en oppdatert oppsummering av hovedaspektene ved sikkerheten og den kliniske ytelsen til FemoSeal™ Vascular Closure System (VCS).

En oppsummering av enhetens sikkerhet og kliniske ytelse, beregnet på brukere/helsepersonell, er tilgjengelig nedenfor i **Avsnitt 1.0**.

## **1.0 OPPSUMMERING FOR BRUKERE/HELSEPERSONELL**

Oppsummeringen av sikkerhet og klinisk ytelse er ikke ment å erstatte bruksanvisningen som hoveddokument for å sikre sikker bruk av enheten, og er heller ikke ment å gi diagnostiske eller terapeutiske forslag til tiltenkte brukere eller pasienter. Oppsummeringen av sikkerhet og klinisk ytelse er ikke ment å erstatte den obligatoriske informasjonen på implantatkortene eller i andre obligatoriske dokumenter.

### **1.1 Tiltent bruk av utstyret**

#### **1.1.1 Bruksområde**

FemoSeal™ Vascular Closure System er en medisinsk enhet som er ment for lukking av en arteriell punksjon etter perkutan kateterisering gjennom hovedlårarterien (arteria femoralis communis).

#### **1.1.2 Bruksindikasjoner**

FemoSeal™ Vascular Closure System er indisert for bruk til lukking av punksjon i hovedlårarterien (arteriotomi) hos pasienter som har gjennomgått perkutan kateterisering med en prosedyrehylse på 7 F (2,33 mm) eller mindre.

#### **1.1.3 Kontraindikasjoner og/eller begrensninger**

FemoSeal™ Vascular Closure System er kontraindisert hos pasienter med arteriotomier der det er brukt hylser eller enheter som er større enn 2,33 mm (7 F).

#### **1.1.4 Tiltent pasientpopulasjon**

Sikkerheten og effekten til FemoSeal™ Vascular Closure System er fastslått hos pasienter på 18 år og eldre som har gjennomgått perkutan kateterisering ved bruk av en prosedyrehylse på 7 F (2,33 mm) eller mindre.

#### **1.1.5 Spesielle pasientpopulasjoner**

Sikkerheten og effekten til FemoSeal™ Vascular Closure System er ikke fastslått i følgende pasientpopulasjoner:

- Pasienter med eksisterende autoimmun sykdom.
- Pasienter som gjennomgår terapeutisk trombolyse.
- Pasienter med klinisk signifikant perifer karsykdom.
- Pasienter med ukontrollert hypertensjon (> 220 mmHg systolisk eller > 110 mmHg diastolisk).

- Pasienter med blødersykdom, inkludert trombocytopeni ( $< 100\,000$  blodplater) eller anemi (Hgb  $< 10$  mg/dl).
- Pasienter med et indre lumen i hovedlårarterien som er mindre enn 5 mm.
- Pasienter med nedsatt nyre- og/eller leverfunksjon.
- Pasienter med annen relevant komorbiditet.
- Populasjoner med spesifikke rasemessige og/eller etniske opprinnelser.
- Pasienter med hjerteinfarkt innen 72 timer.
- Pasienter med et vaskulært transplantat eller en stent på punksjonsstedet.
- Pasienter som er gravide eller ammer.
- Pasienter under 18 år.

### 1.1.6 Tiltente brukere

Tiltente brukere av FemoSeal™ Vascular Closure System er leger med opplæring som kvalifiserer dem til å utføre arteriell tilgang og lukking for endovaskulære prosedyrer gjennom hovedlårarterien, og som har deltatt i et legeinstruksjonsprogram for Terumo Medical Corporation FemoSeal™.

## 1.2 Beskrivelse av utstyret

### 1.2.1 Beskrivelse av utstyret

FemoSeal™ Vascular Closure System, produsert av Terumo Medical Corporation (TMC), er en resorberbar vaskulær lukkeenhet designet for å oppnå femoral arteriell hemostase etter perkutan kateterisering gjennom hovedlårarterien.

FemoSeal™ lukkeelementer består av to resorberbare polymerskiver, den indre forseglingen og den ytre sperreskiven, som holdes sammen av et resorberbart multifilament og dermed forsegler arteriotomien mekanisk (se **Illustrasjon 1.1** og **Illustrasjon 1.2**). Etter å ha blitt plassert gjennom den koniske ytterhylsen, blir den ytre sperreskiven presset på multifilamentskaftet, noe som fører til mekanisk lukking av punksjonsstedet mellom den indre og ytre sperreskiven. Den indre tetningen og den ytre sperreskiven holdes på plass via friksjon på multifilamentskaftet. Hemostase oppnås ved hjelp av mekaniske midler. Lukkeelementene brytes ned ved hydrolyse.

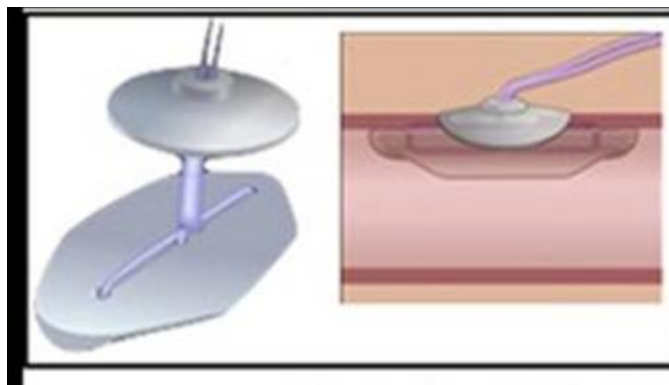
De implanterbare lukkekomponentene, den indre forseglingen og den ytre sperreskiven brytes ned i løpet av atten (18) måneder, mens multifilamentet anslås å bli brutt ned og absorbert via hydrolyse av omkringliggende vev etter to (2) til tre (3) år. De implanterbare lukkekomponentenes evne til å opprettholde kompresjon på arteriotomien er testet ved opptil åtte (8) timer.

Nedbrytningsproduktene metaboliseres og skilles ut i urinen eller går ut som karbondioksid via lungene. Ingen akkumuleringseffekter er observert i dyrestudier. De andre komponentene i FemoSeal™ som vil komme i kontakt med levende vev eller blod under prosedyren, er den koniske ytterhylsen, dilatoren, komprimeringsslangen, pusheren og guidewiren.

### Illustrasjon 1.1 Henholdsvis indre tetning og ytre sperreskive

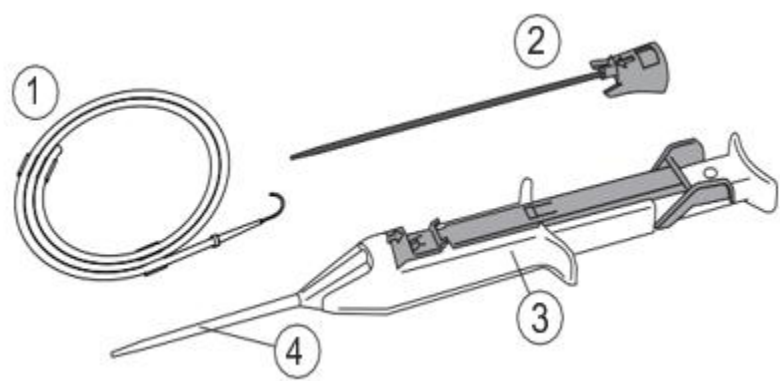


### Illustrasjon 1.2 Plassert indre tetning og ytre sperreskive



FemoSeal™-enheten er pakket sammen med en dilator og en guidewire med 0,038" (0,97°mm) UD, 27,5" (70°cm) lengde og en J-utretter, se **Illustrasjon 1.3** nedenfor. Guidewiren ligger i en polyetylenslange. Alle delene er pakket på et fast papirbrett. Emballasjen inneholder også pasientens implantatkort. FemoSeal™ Vascular Closure System krever ikke ekstra tilbehør for at enheten skal fungere som tiltenkt, og enheten er kun ment for bruk med dilatoren og guidewiren som er inkludert i produktets emballasje.

Illustrasjon 1.3 FemoSeal™ VCS-enhet med guidewire og dilator



1.2.2 Råmaterialer og komponenter

Tabell 1.1 nedenfor viser komponentene i FemoSeal™ VCS.

Tabell 1.1 FemoSeal™ VCS råmaterialer og komponenter

| Delenummer | Beskrivelse                                              |                                                | Materialer                                                                                                                                                                               |
|------------|----------------------------------------------------------|------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1          | 0,038" (0,97 mm) guidewire med J-utretter for guidewiren |                                                | Guidewire: 304 rustfritt stål<br><br>J-utretter: Polypropylen, lilla pigment<br><br>Klips: Polyetylen<br><br>Slange: Polyetylen                                                          |
| 2          | FemoSeal dilator                                         |                                                | Koblingsstykke: Tetrahydrofuran, blått pigment, polybutylen-tereftalat (PBT)<br><br>Slange: Polyetylen med høy tetthet (HDPE), svart pigment<br><br>Smøremiddel: Silikon Dow Corning 360 |
| 3/4        | FemoSeal-enhet                                           | Støpt RD7 – Indre tetning og ytre sperreskive* | Kopolymer mellom glykolid, trimetylenkarbonat, ε-kaprolakton og TMP: trimetylolpropan (initiator)                                                                                        |
|            |                                                          | Multifilament*                                 | Segmentert kopolymer mellom L,L-laktid, trimetylenkarbonat, ε-kaprolakton og 1.3 propandiol (initiator)<br><br>Belegget er kopolymer mellom glykolid, ε-kaprolakton og L-lysin           |
|            |                                                          | Komprimeringsslange                            | Polypropylen                                                                                                                                                                             |

|  |  |                   |                                                 |
|--|--|-------------------|-------------------------------------------------|
|  |  | Pusher            | 304CV rustfritt stål                            |
|  |  | Presse            | Polybutylentereftalat (PBT)                     |
|  |  | Hus               | Polybutylentereftalat (PBT)                     |
|  |  | Knapp             | Polybutylentereftalat (PBT)                     |
|  |  | Knapplokk         | Polyoksymetylen (POM)/polyacetalkopolymer       |
|  |  | Hylse             | Polybutylentereftalat (PBT)                     |
|  |  | Avstandsstykke    | Polybutylentereftalat (PBT)                     |
|  |  | Konus             | Polypropylen                                    |
|  |  | Huslokk           | Polybutylentereftalat (PBT)                     |
|  |  | Sikkerhetshake    | Polybutylentereftalat (PBT), blått pigment      |
|  |  | Hylselokk         | Polybutylentereftalat (PBT)                     |
|  |  | Slangepakning     | Silikon shore A 70                              |
|  |  | Huspakning        | Silikon shore A 50                              |
|  |  | Fjær              | 302 rustfritt stål                              |
|  |  | Konisk ytterhylse | Polypropylen<br>Silikon Dow Corning 360, heksan |

\*Implanterbar del av enheten; implanterbare komponenter er MR-sikre

FemoSeal™ VCS er sterilisert med etylenoksid (EO), og er medisinsk engangsutstyr. FemoSeal™ VCS-enheten er utformet slik at den ikke kan gjenbrukes.

### **Virkemåte**

FemoSeal™ VCS fremmer mekanisk hemostase ved å plassere implanterbare lukkeelementer inne i og utenfor hovedlårarterien. Mekanismen som forhindrer blødning, består av den indre tetningen som forsegler punksjonsstedet, og den ytre sperreskiven som holder den indre tetningen på plass.

### **1.2.3 Klinisk fordel**

FemoSeal™ VCS gir følgende kliniske fordeler med tanke på vaskulær lukking etter punksjon av hovedlårarterien:

- Kortere tid til hemostase<sup>1</sup>
- Kortere tid til ambulerings<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

#### 1.2.4 Tidligere generasjon(er) eller varianter

- Den første versjonen av FemoSeal™ VCS (#11200) ble solgt på det europeiske markedet i 2005 og deler av 2006.
- Den nåværende FemoSeal™ VCS (#11202), med et forbedret innføringssystem, har vært på markedet siden 28. mars 2006.

#### 1.2.5 Tilbehør som er ment for bruk i kombinasjon med enheten

FemoSeal™-enheten er pakket sammen med en dilator, en guidewire med 0,97 mm (0,038") OD og 70 cm (27,5") lengde, og en J-utretter. Guidewiren er tilbehør til FemoSeal™-enheten. J-utretteren er en komponent i guidewiren, mens dilatoren er en komponent i FemoSeal™-enheten. Guidewiren er det eneste tilbehøret som vurderes. Guidewiren ligger i en polyetylenslange. Alle delene er pakket på et fast papirbrett. Emballasjen inneholder også pasientens implantatkort. FemoSeal™ Vascular Closure System krever ikke ekstra tilbehør for at enheten skal fungere som tiltenkt, og enheten er kun ment for bruk med dilatoren og guidewiren som er inkludert i produktets emballasje.

#### 1.2.6 Andre enheter og produkter som er ment for bruk i kombinasjon med enheten

FemoSeal™ VCS krever ikke ekstra utstyr for å fungere som tiltenkt.

### 1.3 Risiko og advarsler

#### 1.3.1 Restrisiko og bivirkninger

Kjente eller forutsigbare bivirkninger, skader og komplikasjoner forbundet med bruk av FemoSeal VCS Vascular Closure Device som følge av restrisiko er oppført i **Tabell 1.2**. Forekomstraten er basert på en analyse av risikodokumentasjonen og beregnet på grunnlag av overvåkingsdata etter markedsføring fra 1. september 2019 til og med 31. august 2024. Det er ingen ukjente restrisikoer for FemoSeal™ VCS, og alle gjeldende risikoer er håndtert gjennom bruksanvisningen og risikostyringsprosessen.



**Tabell 1.2. Bivirkninger/komplikasjoner med FemoSeal**

| Skade                                           | Forekomstrate (%) | Risikoreduserende faktorer                                                                                                                              |
|-------------------------------------------------|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|
| Allergisk reaksjon                              | 0,0000            | Tiltak og planer for å redusere risikoen mest mulig er håndtert via produktets design, produksjonsretningslinjer, produktmerking og opplæring av leger. |
| Aneurisme                                       | 0,0000            |                                                                                                                                                         |
| AV-fistel                                       | 0,0001            |                                                                                                                                                         |
| Blodtap/blødning                                | 0,0280            |                                                                                                                                                         |
| Død                                             | 0,0002            |                                                                                                                                                         |
| Ekkymose                                        | 0,0000            |                                                                                                                                                         |
| Emboli                                          | 0,0000            |                                                                                                                                                         |
| Reaksjon på fremmedlegemer                      | 0,0000            |                                                                                                                                                         |
| Hematom                                         | 0,0027            |                                                                                                                                                         |
| Blødning                                        | 0,0001            |                                                                                                                                                         |
| Infeksjon                                       | 0,0002            |                                                                                                                                                         |
| Inflammatorisk reaksjon                         | 0,0000            |                                                                                                                                                         |
| Nummenhet                                       | 0,0000            |                                                                                                                                                         |
| Smerte                                          | 0,0000            |                                                                                                                                                         |
| Ubehag for pasienten                            | 0,0004            |                                                                                                                                                         |
| Forsinket prosedyre                             | 0,0065            |                                                                                                                                                         |
| Pseudoaneurisme                                 | 0,0004            |                                                                                                                                                         |
| Retroperitoneal blødning                        | 0,0002            |                                                                                                                                                         |
| Sepsis                                          | 0,0000            |                                                                                                                                                         |
| Tromboemboli                                    | 0,0000            |                                                                                                                                                         |
| Trombose                                        | 0,0001            |                                                                                                                                                         |
| Okklusjon av kar / iskemi i nedre ekstremiteter | 0,0002            |                                                                                                                                                         |
| Perforering av kar                              | 0,0000            |                                                                                                                                                         |
| Disseksjon/laserasjon av blodkarvev             | 0,0003            |                                                                                                                                                         |

### 1.3.2 Advarsler og forsiktighetsregler

#### Advarsler

1. Må ikke brukes hvis emballasjen er skadet eller hvis en steril barriere ikke er intakt.
2. Må ikke brukes etter utløpsdatoen – de biologisk nedbrytbare komponentene vil kanskje ikke fungere som de skal.
3. Må ikke brukes hvis noen av delene ser ut til å være skadet eller defekte.
4. Bruk av FemoSeal™ Vascular Closure System der det kan ha oppstått bakteriell kontaminering av prosedyrehylsen eller det omkringliggende vevet, kan forårsake infeksjon.
5. Hvis det er mistanke om at den posteriore arterieveggen er punktert eller at det er utført mer enn én arteriell punksjon, skal du ikke stole på bare FemoSeal™ Vascular Closure System for å oppnå arteriell hemostase. Bruk ytterligere manuell eller mekanisk kompresjon.
6. Hvis punksjonsstedet er ved eller distalt til forgreningen av femoralarterien, skal FemoSeal™ Vascular Closure System ikke brukes på grunn av risikoen for at den indre tetningen plasseres feil. En slik hendelse kan føre til blødningskomplikasjoner og/eller forstyrrelse av den normale blodgjennomstrømningen.
7. Hvis det er vedvarende arteriell blødning fra innsnittstedet, må multifilamentet ikke kuttes før hemostase er oppnådd. Hvis hemostase ikke oppnås, festes multifilamentet med en steril sårbandasje og tilleggskompresjon påføres inntil hemostase er oppnådd. Ved vedvarende arteriell blødning kan det oppstå betydelige blødningskomplikasjoner som kan føre til pasientskade eller død.
8. Ikke bruk FemoSeal™ Vascular Closure System hvis punksjonsstedet er proksimalt for lyskebandet, da dette kan føre til retroperitonealt hematom.
9. Pasienter med høyere risiko for blødning kan få økt blodtap som krever blodoverføring.
10. Hvis den indre skiven løsner, kan det potensielt forårsake en trombotisk og/eller embolisk hendelse.

#### Forholdsregler

1. Plasseringsprosedyren for FemoSeal™ Vascular Closure System skal utføres av leger med tilstrekkelig opplæring i bruk av enheten.
2. Utfør et begrenset femoralt angiogram eller en ultralydveiledet femoralspunksjon før bruk av FemoSeal™ Vascular Closure System.
3. Avbryt prosedyren hvis:

- hovedlårarteriens lumendiameter er  $< 5$  mm.
  - det er stenose og/eller betydelig plakk i nærheten av punksjonsstedet til hovedlårarterien.
  - det er arteriepunksjon ved, eller distalt til, forgreningen av hovedlårarterien.
  - det er uregelmessige grener eller blodkar i nærheten av punksjonsstedet til hovedlårarterien.
4. Hvis det forekommer hematom, må det utvises ekstra forsiktighet for å sikre riktig innføring av den koniske ytterhylsen i arterien.
  5. Bruk punksjonsteknikk for én karvegg. Ikke punkter arteriens bakre karvegg.
  6. Bruk alltid steril teknikk ved bruk av FemoSeal™ Vascular Closure System.
  7. FemoSeal™ Vascular Closure System er kun til engangsbruk, og skal ikke resteriliseres eller gjenbrukes på noen måte. FemoSeal™-enheten er utformet slik at den ikke kan gjenbrukes.
  8. Hvis plasseringen av den indre tetningen møter uventet motstand, må prosedyren avbrytes.
  9. For korrekt plassering av det indre seglet, flytt tommelen slik at knappen kan sprette fritt tilbake.
  10. Sørg for at spissen på den koniske ytterhylsen på FemoSeal™-enheten er under hudoverflaten før den ytre sperreskiven plasseres. Den ytre sperreskiven kan utilsiktet bli plassert over hudnivå hos pasienter med kort avstand mellom lårarterien og hudnivået.
  11. For riktig plassering kan det være nødvendig med et hudinnsnitt før plassering.
  12. Hvis den indre tetningen er inne i arterien, men det ikke er mulig å trykke knappen helt inn og plassere den ytre sperreskiven, kan det være nødvendig med kirurgi for å fjerne lukkeelementene til FemoSeal™.
  13. Hvis det blir nødvendig med ny punksjon av den samme lårarterien innen 18 måneder, skal den nye punksjon utføres minst én centimeter proksimalt for det forrige tilgangsstedet for FemoSeal™ Vascular Closure System.
  14. Be pasienten følge legens anvisninger angående inspeksjon av lukkestedet.
  15. Be pasienten ha med seg pasientinformasjonskortet i de neste 18 månedene

### **Forholdsregler ved utskriving**

Før utskriving vurderes, må pasienten vurderes for følgende kliniske tilstander:

1. Blødning og/eller hematom på lukkestedet.

2. Smerte ved gange.
3. Tegn på infeksjon ved lukkestedet.

### 1.3.3 Korrigerende feltsikkerhetstiltak

Det var ett korrigerende feltsikkerhetstiltak som involverte FemoSeal™ VCS i perioden fra 1. september 2019 til og med 31. august 2024.

I 2022 tilbakekalte Terumo frivillig FemoSeal™ VCS på grunn av klager på feil i prosess- og partifrigjørings tester av Elkton-produserte FemoSeal-produkter for måling av støtkraft og tilbaketrekingskraft. Totalt ble 950 enheter tilbakekalt fra Sør-Korea.

## 1.4 Oppsummering av klinisk evaluering og klinisk oppfølging etter markedsføring

**Tabell 1.3** inkluderer en liste over vesentlige studier som er inkludert for å lansere FemoSeal™ VCS på markedet, samt studier etter markedsføring og kliniske oppfølgingsaktiviteter etter markedsføring. Enhetsversjonen som ble anvendt i studien, er inkludert i tabellen nedenfor. Den første versjonen av FemoSeal™ VCS (#11200) var på markedet frem til 2006, mens den neste versjonen (#C11202) ble lansert på markedet i 2006 og er den som er på markedet i dag.

**Tabell 1.3 Oppsummering av vesentlige studier**

| Funksjonell dyretesting før markedsføring                                                                                                                                                                                                                               | Enhetsversjon               |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                       |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                       |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                       |
| Første klinisk studie på mennesker                                                                                                                                                                                                                                      |                             |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                       |
| Fullførte kliniske studier etter markedsføring                                                                                                                                                                                                                          |                             |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                                                                              | C11202<br>(gjeldende enhet) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                                                                                       | C11202<br>(gjeldende enhet) |

|                                                                                                                                 |                             |
|---------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | C11202<br>(gjeldende enhet) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)          | C11202<br>(gjeldende enhet) |
| <b>Planlagte/pågående kliniske studier etter markedsføring</b>                                                                  |                             |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                      | C11202<br>(gjeldende enhet) |
| <b>Kliniske oppfølgingsaktiviteter etter markedsføring</b>                                                                      |                             |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(gjeldende enhet) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(gjeldende enhet) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(gjeldende enhet) |

### 1.4.1 Oppsummering av data før markedsføring (dyrestudier og kliniske undersøkelser)

**Tabell 1.4** nedenfor beskriver alle studier før markedsføring, både på dyr og kliniske undersøkelser.

**Tabell 1.4 Oppsummeringer av undersøkelser før markedsføring**

| Funksjonell dyretesting før markedsføring                                                                                                                                                                                                                            |                                                                      |                                      |                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                         |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------|--------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Studiens navn                                                                                                                                                                                                                                                        | År / CI                                                              | Type studie                          | Målsetninger                                                                                                                                                                                                                                              | Milepæler                                                                                                                                                                                                                                                          | Potensielle akseptkriterier                                                                                                                                                                                                                                                                                                                                                             |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 2000<br>Radi Medical System AB<br><br>Utført av Biomatech, Frankrike | Dyrestudie; Eksplorativ undersøkelse | Formålet med studien var å evaluere biokompatibiliteten og biofunksjonaliteten til et biologisk nedbrytbart implantat designet for å oppnå hemostase i det vaskulære systemet. Rapporten omhandler reservedyr fra studienummer 862 (dokument nr. 1051-01) | N = 3 voksne hunnsauer, 1 dyr per tidspunkt<br><br>Oppfølging for histopatologisk analyse, makroskopisk gradering og ultrastrukturell analyse<br><br>• 12 måneder<br>• 15 måneder<br>• 18 måneder<br><br>Oppfølging med doppler-ultral lyd i farger – 30 dager ved | Arteriell åpenhet<br>• Vurdering av blodgjennomstrømning etter plassering – 2/3 reduksjon av blodgjennomstrømning forbundet med midlertidig arteriell vasospasme som ble tilskrevet prosedyren, begge forekom ved venstre halsarterie<br>• Vurdering av doppler-ultral lyd (4 uker) med farger – 3/3 (100 %) uten kraftig reduksjon av blodgjennomstrømning 30 dager etter implantasjon |

|  |  |  |  | tilgangssteder for hals- og<br>lårarterier | <p>Makroskopiske observasjoner</p> <ul style="list-style-type: none"> <li>12 måneder – åpenhet bekreftet makroskopisk ved fravær av anatomisk synlig okklusjon; ingen makroskopiske lokale intoleranselesjoner (blødning, nekrose eller neovaskularisering); innkapsling av indre skive syntes å være markert</li> <li>15 måneder – makroskopisk observasjon viste ingen tegn på inflammasjon; ingen rester av indre eller ytre skiver identifisert; innkapslingsvev i området rundt ytre skive så ut til å være det samme som 12 måneders observasjon</li> <li>18 måneder – makroskopisk observasjon viste ingen tegn på lokal intoleranse, ytre skive synlig (3/3 tilfeller), nedbrytning av indre skive komplett, 1/3 (venstre halsarterie) – depresjon av arterieveggen observert på implantatstedet (kan være relatert til plassering av enheten)</li> </ul> <p>Konklusjoner</p> <ul style="list-style-type: none"> <li>Makroskopisk ble det 12, 15 og 18 måneder etter implantasjon ikke påvist noen nekrotiske, degenerative eller trombotiske tegn.</li> <li>Nedbrytningsprosessen for de indre og ytre skivene så ut til å pågå mellom 12 og 18 måneder, og så ut til å være fullført etter 18 måneder, med et hvitaktig vev som dekket det implanterte området.</li> <li>Histologisk var polymermaterialet ikke lenger synlig etter 18 måneder, men endoluminalt fibrøst vev forekom. Ingen nekrotiske, degenerative eller trombotiske lesjoner ble observert.</li> </ul> |
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|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|---------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002 Radi Medical System AB</p> <p>Utført av Biomatech, Frankrike</p> | <p>Dyrestudie; Eksplorativ undersøkelse</p> | <p>Formålet med studien var å evaluere biokompatibiliteten til et biologisk nedbrytbart implantat som ment for å oppnå hemostase i det vaskulære systemet.</p> | <p>Oppfølging (etter implantasjon)</p> <ul style="list-style-type: none"> <li>• 12 uker</li> <li>• 24 uker</li> <li>• 36 uker</li> </ul> <p>N = 12 sauer, 3 dyr per tidspunkt, 3 reservedyr ofret ved 12, 15 og 18 måneder</p> <p>Implantasjonssteder – høyre og venstre lårarterie, høyre og venstre halsarterie</p> <p>Doppler-ultralydanalyse med farger</p> | <p><u>Åpenhet i hals- og femoralarteriene etter 4 uker</u></p> <ul style="list-style-type: none"> <li>• Stor reduksjon i blodgjennomstrømning 0/12 (0 %)</li> </ul> <p><u>Ingen stor reduksjon av blodgjennomstrømningen</u></p> <ul style="list-style-type: none"> <li>• Alvorlig nedsatt blodgjennomstrømning relatert til innsetting av enheten 0/12 (0 %)</li> <li>• Redusert blodstrøm i venstre karotid 2/12 (16,6 %) på grunn av midlertidig arteriell vasospasme (tilskrevet kirurgi, ikke enheten)</li> </ul> <p><u>Nedsatt blodgjennomstrømning ved oppfølging</u></p> <p>12 uker – 0/12 (0 %)</p> <p>24 uker – 0/12 (0 %)</p> <p>36 uker – 0/12 (0 %)</p> <p>Blodtrykksmålinger (3 sauer – 36 uker)</p> <ul style="list-style-type: none"> <li>• Ingen større reduksjon i blodgjennomstrømning registrert</li> </ul> <p>Makroskopiske data for integrasjon og nedbrytning (grad 0–4)</p> <p><u>Halsarterie-plassering</u></p> <p><u>Innvendig side</u></p> <p>-innkapsling</p> <p>12 uker 1,3</p> <p>24 uker 0,8</p> <p>36 uker 0,7</p> <p>- materialnedbrytning</p> <p>12 uker 2,2</p> <p>24 uker 2,3</p> <p>36 uker 0,7</p> <p><u>Utvendig side</u></p> <p>-innkapsling</p> <p>12 uker 2,0</p> <p>24 uker 1,0</p> <p>36 uker 0,8</p> <p>- materialnedbrytning</p> |
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|  |  |  |  |  | 12 uker 2,0<br>24 uker 2,7<br>36 uker 3,2<br><br><u>Lårarterieplassering</u><br><i>Utvendig side</i><br>-innkapsling<br>12 uker 1,0<br>24 uker 2,7<br>36 uker 1,0<br>- materialnedbrytning<br>12 uker 2,0<br>24 uker 2,4<br>36 uker 3,0<br><br><i>Innvendig side</i><br>-innkapsling<br>12 uker 2,0<br>24 uker 1,2<br>36 uker 1,0<br>- materialnedbrytning<br>12 uker 1,0<br>24 uker 2,2<br>36 uker 3,0<br><br><u>Histologiske data for integrering, nedbrytning og inflammatoriske parametere (gjennomsnitt av relevante verdier, indeks 0-4) n=6</u><br><br><u>Halsarterieplassering</u><br>Ekstern fibrose<br>12 uker – 2,3<br>24 uker – 2,3<br>36 uker – 1,8<br>Intern neointima<br>12 uker – 3,0<br>24 uker – 2,7<br>36 uker – 3,3<br>Materialnedbrytning<br>12 uker – 1,7<br>24 uker – 3,0<br>36 uker – 3 +<br>Inflammatoriske parametre (makrofager)<br>12 uker – 3,0<br>24 uker – 1,7<br>36 uker – 1,7<br><br><u>Lårarterieplassering</u><br>Ekstern fibrose |
|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|



|  |  |  |  |  | 12 uker – 1,3<br>24 uker – 1,5<br>36 uker – 1,7<br>Intern neointima<br>12 uker – 3,7<br>24 uker – 3,3<br>36 uker – 3,8<br>Materialnedbrytning<br>12 uker – 2,0<br>24 uker – 3,0<br>36 uker – 3+<br>Inflammatoriske parametre<br>(makrofager)<br>12 uker – 3,5<br>24 uker – 1,8<br>36 uker – 1,8<br><br><u>Histomorfologiske<br/> åpenhetsverdier</u><br>Halsarterieplassering<br>12 uker 74,0 %<br>24 uker 81,9 %<br>36 uker -89,43%<br>Lårarterieplassering<br>12 uker – 42,2 %<br>24 uker – 73,21 %<br>36 uker – 78,71 %<br><br><u>US karåpenhet (gjennomsnitt<br/> %)</u><br>Halsarteriested<br>12 uker 94,6 %<br>24 uker – 96,7 %<br>36 uker – 94,7 %<br>Lårarterieplassering<br>12 uker – 66,9 %<br>24 uker – 63,6 %<br>36 uker – 75,1 %<br><br>Konklusjoner <ul style="list-style-type: none"> <li>Ingen signifikante lokale tegn på intoleranse ble påvist (fravær av synlige inflammatoriske, nekrotiske eller degenerative lesjoner) ved 12, 24 eller 36 uker</li> <li>Ingen signifikante bivirkninger knyttet til vert og enhet ble registrert</li> <li>Nedbrytningen av implantatet var nesten fullført etter 36 uker</li> </ul> |
|--|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                                                                                                                                                                                                                                                                 |                                                                          |            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France). | 2002<br><br>Radi Medical System AB<br><br>Utført av Biomatech, Frankrike | Dyrestudie | Formålet med studien var å evaluere biokompatibiliteten og biofunksjonaliteten til et biologisk nedbrytbart implantat designet for å oppnå hemostase i det vaskulære systemet. Den testede enheten var ment å føres inn i punksjonshullet i arteriene for å oppnå hemostase. Den ene skiven gikk inn i punksjonshullet i arterien, og den andre strammet den indre skiven fra utsiden av arterien. Begge skivene ble ført inn gjennom en innføringshylse. Skivene ble designet for å forhindre blødning, for å leges inn i karveggen og til slutt brytes de ned og absorberes. Studien var utformet for å samle inn og analysere data etter funksjonell implantasjon hos sau og gris for å evaluere implantatets kapasitet til å opprettholde fysiologisk funksjon ved bruk i sirkulasjonssystemet, for å bestemme vertens respons og enhetens respons (fysisk integritet, vevsinnekapling ved ofring) og for å evaluere nedbrytningen av implantatet | Implantasjonsperiode/oppfølging er 5 uker for alle dyr<br><br>4 sauer, 1 gris<br><br>14 lukkeelementer<br><br>8 lukkeelementer implantert i 2 sauer,<br><br>2 lukkeelementer implantert i 1 gris<br><br>Når to lukkeelementer ble implantert i samme femoralarterie, ble de implantert med en avstand på > 30 mm | Eventuelle bivirkninger (inflammasjon, nekrose, blødning eller andre lesjoner) eller eventuell tynn pseudointimal lagdannelse ble registrert. Det ble lagt spesiell vekt på første vevsintegrering av enheten, med spesiell vekt på innkapslingen av den innvendige skiven.<br><br>Makroskopisk ble det ikke observert signifikante tegn på lokal intoleranse eller trombedannelse. Den makroskopiske observasjonen viste ingen forskjell mellom sauen eller grisen etter implantasjon av lukkeelementene i lårarteriene. Makroskopisk ble det ikke observert signifikante tegn på lokal intoleranse eller trombedannelse. Den makroskopiske observasjonen viste ingen forskjell mellom sauen eller grisen etter implantasjon av lukkeelementene i lårarteriene.<br><br>Den histopatologiske analysen av implantasjonsstedet hos sau viste ingen lokale bivirkninger. De indre og ytre skivene viste tegn på nedbrytning og ble i noen tilfeller brutt ned i mindre deler. De indre skivene var fullstendig integreert i neointimalt vev. Hos grisen viste den histopatologiske analysen litt mer inflammatoriske tegn rundt de indre og ytre |
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|                                                                                                                                                                                                              |                              |                                   |                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                               | <p>skivene. Hos begge dyr viste multifilamentet litt flere inflammatoriske tegn enn hos skivematerialet, noe som er normalt for flettede suturer på grunn av det større overflateområdet.</p> <p>Karets åpenhet ble målt etter 5 uker ved bruk av tre ulike metoder, histomorfometrisk, histomorfometrisk i kombinasjon med måling av kardiameter ved bruk av skyvelære og ved bruk av doppler-ultralyd med farger. Gjennomsnittlig åpenhet i blodkar hos sau var mellom 60 og 80 %, avhengig av metode (12 observasjoner). Hos grisen var middelverdi for åpenhet i blodkar mellom 40 og 80 % (2 observasjoner).</p> |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Første klinisk studie på mennesker</b>                                                                                                                                                                    |                              |                                   |                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Studiens navn                                                                                                                                                                                                | År / CI                      | Type studie                       | Målsetninger                                                                                                                                                                                                                                                                                | Milepæler                                                                                                                                                                                                                                                                                                                                     | Potensielle akseptkriterier                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Åpen, enkeltarm multisenterstudie | Formålet med studien var å bestemme sikkerhet, ytelse og effekt av FemoSeal Vascular Closure System (FemoSeal-system) generelt, og spesielt lukkeelementene, hos pasienter som gjennomgår hjertediagnostiske eller intervensjonelle kardiologiske prosedyrer ved bruk av lårarterietilgang. | <p>2-delt studie</p> <p>Totalt n = 80</p> <p>Del 1 n = 20</p> <p>Del 2 n = 60</p> <p>Indikasjoner:</p> <p>Del 1 – diagnostisk hjertekateterisering med lårarterie som tilgangssted</p> <p>Del 2 – pasienter som gjennomgår diagnostiske og intervensjonelle hjerteprosedyrer med lårarterien som tilgangssted</p> <p>30 dagers oppfølging</p> | <p>Resultater</p> <p><u>Hemostase oppnådd med FS uten kompresjon</u></p> <p>- Del 1 20/20 (100 %)</p> <p>- Del 2 58/60 (97 %)</p> <p>Mediantid til hemostase ved prosedyren (del 2) – 1,0 minutter (område umiddelbart – 8 minutter)</p> <p><u>Tid til ambulering (minutter)</u></p> <p>Del 1 – Median: 33,0</p> <p>Gjennomsnitt: 67,8</p> <p>Del 2 – Median: 45</p>                                                                                                                                                                                                                                                  |

|  |  |  |  |  | Gjennomsnitt: 87,5<br><br><u>Forekomst av større vaskulære komplikasjoner – 30 dagers oppfølging</u><br>Del 1<br>-Uten vaskulære komplikasjoner 20/20 (100 %)<br>Del 2<br>Pseudoaneurisme – 1/59 (1,69 %)<br><br><u>Mislykket behandling</u><br>Del 1 – 0/20 (0 %)<br>Del 2 – 3/60 (5 %) <ul style="list-style-type: none"> <li>• 2 på grunn av manglende hemostase uten bruk av kompresjon</li> <li>• 1 på grunn av alvorlig vaskulær komplikasjon, pseudoaneurisme</li> </ul><br><u>Varig væsning</u><br>Del 1 – 0/20 (0 %)<br>Del 2 – 8/60 (13 %)<br><br><u>Hematom</u><br>Del 1 – 0/20 (0 %)<br>Del 2 – 6/60 (10 %) |
|--|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Som en del av utviklingsplanen før markedsføring av FemoSeal™ VCS, ble det gjennomført 3 funksjonelle tester på dyr. I 2000, før oppstart av kliniske studier, ble det utført en dyrestudie for å evaluere biofunksjonaliteten til FemoSeal™ VCS. Denne studien evaluerte lukkeelementenes kapasitet til å opprettholde fysiologisk funksjon, og evaluerte nedbrytningen av dem. Ved 18 måneder var det indre og ytre skivematerialet ikke lenger synlig, etter å ha blitt erstattet med et endoluminalt fibrøst vev. Konklusjonen var at FemoSeal™ VCS-lukkeelementets kapasitet til å opprettholde fysiologisk funksjon når det brukes i sirkulasjonssystemet, ble bekreftet.

I 2002 ble det utført en dyrestudie for å evaluere biokompatibiliteten og biofunksjonaliteten til et biologisk nedbrytbart implantat, FemoSeal™ VCS, designet for å oppnå hemostase i det vaskulære systemet. Kort oppsummert var nedbrytningen av implantatet nesten fullstendig etter 36 uker, og det var ingen signifikant vevsreaksjon.

En annen dyrestudie i 2002 evaluerte biokompatibiliteten og biofunksjonaliteten til et biologisk nedbrytbart implantat, FemoSeal™ VCS, designet for å oppnå hemostase i det vaskulære systemet. Etter 5 uker var innkapslingen av skiven fullført, og tegn på nedbrytning ble observert for indre og ytre skiver. Konklusjonen var at implantatets kapasitet til å opprettholde fysiologisk funksjon når det ble brukt i sirkulasjonssystemet, ble bekreftet.

Som en del av den kliniske utviklingsplanen for FemoSeal™ VCS utførte Radi Medical System AB en klinisk undersøkelse før markedsføring. Denne kliniske undersøkelsen er ikke publisert eller tilgjengelig på nettet. Studien med enhetsmodell #11200 ble utført i 2002–2004 under europeisk standard EN 540 (Klinisk undersøkelse av medisinsk utstyr for mennesker) og i samsvar med ICH General Considerations for Clinical Trials and Guideline for Good Clinical Practice. Detaljene i denne studien er dokumentert i rapport EU-SE-001. Den kliniske studien ble dokumentert i den endelige rapporten fra Radi Medical Systems AB; "Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures". Den kliniske studien ble utført med den første modellen av FemoSeal™, nr. 11200, og fokuserte på sikkerheten og effekten til de implanterbare lukkekomponentene. Den eneste forskjellen mellom den første modellen, nr. 11200, og den nåværende modellen, C11202, er den franske størrelsen, henholdsvis 6 F og 7 F, og det forbedrede innføringssystemet. De kliniske fordelene, tiltenkt bruk, operasjonsprinsipper og råmaterialene i de implanterbare lukkeelementene, den indre forseglingen og den ytre sperreskiven forblir uendret.

Tiltenkt bruk av enheten var for pasienter som gjennomgikk diagnostiske hjerteprosedyrer eller intervensjonelle hjerteprosedyrer med lårarterien som et tilgangspunkt. Formålet med denne studien var å fastslå sikkerhet, ytelse og effekt av FemoSeal™ VCS. Dette var en prospektiv, multisenter, enkeltarm, åpen studie med 30 dagers oppfølging.

Det primære ytelsesendepunktet var tid til hemostase definert som fravær av aktiv blødning. Det primære sikkerhetsendepunktet var forekomst av alvorlige vaskulære komplikasjoner i løpet av 30 dager. Sekundære endepunkter inkluderte tid til ambulering, andel behandlingssvikt, forekomst av bivirkninger og enhetens ytelseskarakteristikker under innføring og plassering.

Pasientene i denne studien var voksne som var i stand til å gi informert samtykke, og med minst én intakt pedalpuls. Pasientene ble ekskludert fra studien hvis de hadde noen av følgende tilstander:

- Tidligere perifer karsykdom
- Autoimmune sykdommer

- Kjent blødningsforstyrrelse eller alvorlig anemi
- INR >1,5
- Hjerteinfarkt de siste 72 timer
- Ukontrollert hypertensjon til tross for behandling
- Fedme som hindret tilgang med Seldinger-teknikk
- Tilstedeværelse av vaskulært transplantat eller en stent på arteriotomistedet
- Tidligere ipsilateral punksjon innen 3 måneder
- Forventet levetid < 6 måneder

I tillegg ble pasientene undersøkt intraoperativt og ekskludert fra studien hvis noe av det følgende ble observert:

- Hovedlårarteriens lumendiameter < 5 mm
- Arteriegrener innen 2 cm proksimalt for punksjonsstedet
- Signifikant stenose innen 3 cm fra punksjonsstedet
- Bruk av primær innføringshylse > 6 Fr
- Punktering ved eller distalt for forgreningen av lårarterien
- Flere punksjoner i lårarterien
- Kjent eller mistenkt posterior punksjon av lårarterieveggen
- Stort hematom (2:6 cm) ved fullføring av prosedyren
- Vanskelig innføring av primærhylse for prosedyre på grunn av buktende vev eller blodkar

Denne enkeltprotokollstudien ble utført i to deler: 20 pasienter ble inkludert i del 1, deretter ble det utført en sikkerhetsanalyse, og deretter ble ytterligere 60 pasienter inkludert i del 2.

I del 1 var gjennomsnittlig alder for inkluderte pasienter 65,9 år, 70,0 % av pasientene var menn og 95 % av pasientene brukte samtidig medisiner. I del 2 av studien var gjennomsnittsalderen 63,8 år, 78 % var menn og 100 % brukte samtidig medisiner.

Pasienter som gjennomgikk diagnostiske (del 1 og del 2) eller intervensjonelle (del 2) hjertekateteriseringsprosedyrer, var kvalifisert for deltakelse i studien. Prosedyrene var i samsvar med standard pleie ved hvert av de deltagende sykehusene, etterfulgt av bruk av FemoSeal™ VCS. Pasientdata ble samlet inn ved baseline, under prosedyren og 1 dag og 30 dager etter prosedyren. Resultatene er oppsummert i **tabell 1.5** og indikerer at FemoSeal™ VCS er sikker og effektiv for bruk i denne pasientpopulasjonen.

**Tabell 1.5 Kliniske resultater rapportert i studien før markedsføring**

|                                                                                                                   | Del 1         | Del 2                      |
|-------------------------------------------------------------------------------------------------------------------|---------------|----------------------------|
| Antall pasienter                                                                                                  | 20            | 60                         |
| Gjennomsnittlig tid til hemostase                                                                                 | 1,2 minutter  | 1,6 minutter <sup>a</sup>  |
| Gjennomsnittlig tid til ambulering                                                                                | 72,2 minutter | 87,5 minutter <sup>b</sup> |
| Forekomst av større vaskulære komplikasjoner <sup>c</sup>                                                         | 0 (0 %)       | 1 (2 %)                    |
| Antall pasienter med bivirkninger                                                                                 | 5 (25 %)      | 19 (32 %)                  |
| Behandlingsfeil (definert som alvorlige vaskulære komplikasjoner, behov for manuell kompresjon eller begge deler) | 0 (0 %)       | 3 (5 %)                    |
| Feil på enheten                                                                                                   | 0 (0 %)       | 6 (10 %)                   |

<sup>a</sup>Basert på en total prøvestørrelse på 58 fordi 2 pasienter ikke oppnådde hemostase på prosedyretidspunktet på grunn av tidligere ipsilaterale punksjoner. Hemostase ble oppnådd etter 7 minutter og 37 minutter for disse pasientene.

<sup>b</sup>Basert på total prøvestørrelse på 59: 1 pasient ble ikke inkludert fordi pasienten ble lagt i respirator på grunn av lungeødem og ikke kunne ambulere på over en uke.

<sup>c</sup>Definert som vaskulær komplikasjon som krever blodtransfusjon eller kirurgisk reparasjon, eller lokal infeksjon som krever administrasjon av antibiotika, sykehusinnleggelse eller forlengelse av sykehusoppholdet, eller debridering av stedet

Ingen større vaskulære komplikasjoner ble observert i del 1 av studien. Det ble rapportert om 1 større vaskulær komplikasjon i del 2 av studien: pseudoaneurisme som ble rapportert innen 1 dag etter prosedyren. Hendelsen krevde ultralydveiledet kompresjon og en injeksjon av trombin i pseudoaneurismen, og forlenget pasientens sykehusopphold.

Av de 5 bivirkningene som ble rapportert i del 1 av studien, var det én mulig utstyrsrelatert bivirkning: en ikke-alvorlig hendelse med aktiv blødning 1 dag etter prosedyren. Av de 19 bivirkningene som ble rapportert i del 2 av studien, ble det observert 3 enhetsrelaterte, ikke-alvorlige bivirkninger med hematom, og 6 mulige enhetsrelaterte ikke-alvorlige hendelser ble observert, inkludert 3 rapporter om vedvarende væsning, 2 hematomer og 1 bensmerte etter trening.

Det var 3 pasienter i del 2 som ble vurdert som mislykket behandling: 2 på grunn av manglende hemostase uten bruk av kompresjon og 1 på grunn av den store vaskulære komplikasjonen (pseudoaneurisme). Det var ingen behandlingssvikt i del 1 av studien.

Av de seks enhetsfeilene i del 2 av studien forstyrret tre ikke prosedyren. Én av dem skyldtes brukerfeil, én var lekkasje i innføringenheten og én var et ødelagt filamentledd. De to siste problemene ble løst med modelloppdateringene som er implementert i C11202.

Del 2 av den kliniske studien før markedsføring rapporterte ikke resultatene av oppfølging etter 6 måneder på grunn av manglende etterlevelse hos pasienten. Resultatene av den kliniske studien før markedsføring (EU-SE-001) etter 30 dager, som er i tråd med oppfølgingsperioden i klinisk litteratur, viser at FemoSeal™ VCS er trygt og effektivt.

### 1.4.2 Oppsummering av data fra kliniske studier etter markedsføring

Det ble utført 4 fullførte kliniske studier etter markedsføring, beskrevet i **Tabell 1.6** nedenfor. Disse kliniske undersøkelsene er ikke publisert eller tilgjengelige på nettet.

**Tabell 1.6 Kliniske studier etter markedsføring**

| Fullførte kliniske studier etter markedsføring                                              |                                                              |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                      |
|---------------------------------------------------------------------------------------------|--------------------------------------------------------------|--------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Studiens navn                                                                               | År / CI                                                      | Type studie                                                        | Målsetninger                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Milepæler                                                                                                                                                                                                                                                                                                                      | Potensielle akseptkriterier                                                                                                                                          |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI                                                 | Studie etter markedsføring, brukerakseptabilitet for ny emballasje | Studie etter markedsføring utført på modelloppdateringen FemoSeal Vascular® Closure System nr. 11202 som har et modifisert leveringssystem sammenlignet med den første modellen, nr. 11200, for å dokumentere funksjonaliteten. Formålet med studien var å få tilbakemelding på den reviderte bruksanvisningen, opplæringsprosjektet for leger og sykepleiere, for å bekrefte vurderingene som er gjort i risikoanalysen og å gi innspill til eventuelle kvalitetsforbedringer av produktene. | 100 pasienter <ul style="list-style-type: none"> <li>63 menn / 37 kvinner</li> <li>Gjennomsnittsalder 68 år for kvinner, 65 år for menn</li> </ul> 2 svenske sykehus, 6 leger<br><br>112 enheter<br><br>Data registrert i pasientjournal-skjemaer (CRF)<br><br>Planlagt observasjonstid – 30 minutter fra påføringstidspunktet | Resultater<br><br>1. Illustrasjonene/ instruksjonene i bruksanvisningen anses som informative og tilstrekkelige<br><br>2. Umiddelbar hemostase (91/100)              |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)           | Dr. Nicolas Moes Innsbruck medisinske universitet, Østerrike | Bekreftelsesvurdering etter markedsføring                          | Formålet med denne studien var å vurdere sikkerheten og ytelsen til FemoSeal® brukt under normal klinisk rutine hos pasienter som gjennomgår diagnostisk                                                                                                                                                                                                                                                                                                                                      | 50 etterfølgende pasienter<br><br>Indikasjon – diagnostisk eller invasiv hjertekateterisering fra hovedårarterie                                                                                                                                                                                                               | Primære endepunkter <ul style="list-style-type: none"> <li>Primært effektendepunkt – TTH (tid til hemostase) med eller uten væsning, men uten ytterligere</li> </ul> |



|                                                                                |            |                            |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
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|                                                                                |            |                            | <p>hjerterkateterisering eller perkutant hjersteinngrep utført med 7 F-hylse.</p>                                                                                                                                                                                                                                                 | <table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                                                                                                                                                                                                                                 | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | <ul style="list-style-type: none"><li>• kompresjon, manuell eller mekanisk.</li><li>• Sikkerhetsendepunkt – forekomst av bivirkninger – mindre og større vaskulære komplikasjoner og alle andre bivirkninger – alvorlige og ikke alvorlige under hele studiens varighet (dvs. til pasienten skrives ut).</li></ul> <p>Resultater</p> <ul style="list-style-type: none"><li>• Gjennomsnittlig tid til hemostase</li><li>• Diagnose – 56,6 ± 29 sekunder</li><li>• Intervensjonell 59,9 ± 16,2 sekunder</li><li>• Alle pasienter 57,8 ± 26,3</li><li>• Alle pasienter kunne uten problemer ambuleres etter 4 timers hvile i sengen.</li></ul> <p>Sikkerhetsresultater</p> <ul style="list-style-type: none"><li>• 49/50 (98 %) fri for vaskulære komplikasjoner frem til utskriving fra sykehuset</li><li>• Gjennomsnittlig tid til utskriving 2,6 dager</li><li>• 1/50 (2 %) mindre blødning neste dag etter udramatisk ambulering på samme dag som angiografien</li></ul> |
| n                                                                              | 50         |                            |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| men                                                                            | 35 (70%)   |                            |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| women                                                                          | 15 (30%)   |                            |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| PCI cases                                                                      | 15         |                            |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| age (yrs)                                                                      | 62.8±11.1  |                            |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| body mass index (kg/m²)                                                        | 25.4±6.7   |                            |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| systolic BP (mmHg)                                                             | 131.2±20.9 |                            |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| diastolic BP (mmHg)                                                            | 77.9±10.6  |                            |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| diabetes mellitus                                                              | 9 (18%)    |                            |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| arterial hypertension                                                          | 34 (68%)   |                            |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| previous coronary intervention                                                 | 13 (26%)   |                            |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| preprocedure aspirin                                                           | 50 (100%)  |                            |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| preprocedure clopidogrel                                                       | 50 (100%)  |                            |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Procedural unfractionated heparin                                              | 15 (30%)   |                            |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Procedural abciximab                                                           | 2 (4%)     |                            |                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009) | 2009 RADI  | Studie etter markedsføring | <p>Studien skal informere om kundene/brukerne opplevde problemer med den nye emballasjen, spesielt den usterile utsiden av Tyvek/PET-PE-posen.</p> <p>Studien skal også gi informasjon om hvorvidt behandlende lege oppfatter noen forskjeller i enhetens bruksmåte/innføringsmåte sammenlignet med tidligere brukte enheter.</p> | <p>25 enheter</p> <p>4 svenske sykehus</p> <p>16/25 (64 %) av pasientene var PCI-pasienter med tunge antikoagulasjonsmedisiner</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <p>Resultater</p> <p>1. Pakkerelaterte problemer – 21/25 (84 %) bruksområder var vellykkede; 4/25 (16 %) var mislykkede (1 – testing av ny innføringsenhet, 1 indre skive gikk gjennom arteriotomi ved tilbaketrekking, knappen kom opp og den ytre skiven ble plassert i snittvevskanalen, 2 umiddelbar hemostase ble ikke oppnådd til tross</p> |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |

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|---------------------------------------------------------------------------------------------------------------------------------|----------------------------------|-----------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                 |                                  |                                                                 | Studien skal også gi innspill til eventuelle videre behov for kvalitetsforbedringer.                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                    | for ingen problemer med plassering.)<br>2. Umiddelbar hemostase 19/25 (76 %) pasienter<br>3. Blødning 11/25 (44 %) – 9/25 (36 %) utflod/blødning, 2/25 (8 %) hematomer<br>Total hendelsesrate 19 %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022) | 2022/ Terumo Medical Corporation | Prospektiv, multisenter, observasjonsstudie etter markedsføring | For ytterligere å demonstrere sikkerheten og effekten til FemoSeal™ VCS gjennom oppnådd hemostase i vanlige tilgangssteder for hovedlårarterier hos reelle forsøkspersoner som gjennomgår perkutane endovaskulære prosedyrer. | <ul style="list-style-type: none"> <li>Pasientoppfølging etter 30 dager (± 7 dager) ved sykehusbesøk eller telefonsamtale.</li> <li>Innlogging: Desember 2021 til juli 2022.</li> <li>230 registrerte forsøkspersoner som gjennomgår diagnostiske eller intervensjonelle endovaskulære prosedyrer der FemoSeal™ brukes.</li> </ul> 3 europeiske steder: Frankrike (92 pasienter), Tyskland (38 pasienter), Belgia (100 pasienter). | <ul style="list-style-type: none"> <li><b>Demografi/ komorbiditeter:</b> <ul style="list-style-type: none"> <li>- Kjønn: 161 menn (70 %) / 69 kvinner 69 (30 %).</li> <li>- Gjennomsnittlig alder: 70 ± 12.</li> <li>- KMI: 26,1 ± 4,95 kg/m2.</li> <li>- Hypertensjon: 160 pasienter (69,6 %).</li> <li>- Dyslipidemi: 128 (55,7 %).</li> <li>- Koronararteriesykdom: 42 (18,3 %).</li> <li>- Nåværende røyker: 86 (37,6 %).</li> <li>- Tidligere røyker: 66 (28,8 %).</li> <li>- Koronar hjertesykdom: 34 (14 %).</li> <li>- Tidligere myokardinfarkt: 18 (7,8 %).</li> <li>- Revaskularisering av perifer arterie: 12 (5,2 %) halsarterie og 83 (37,5 %) og arteria labialis.</li> <li>- Blodplatehemmende behandling (ved baseline): 211 (91,7 %), inkludert 21 (9,1 %) dobbel blodplatehemmende behandling (DAPT).</li> <li>- Oral antikoagulant: 40 (17,4 %) pasienter.</li> </ul> </li> <li><b>Prosedyrekarakteristikk er:</b> <ul style="list-style-type: none"> <li>- Miljø: innlagt klinikk 162 tilfeller (70,4 %), poliklinikk 68 tilfeller (29,6 %).</li> <li>- Vedvarende indikasjon: klaudikasjon 147 tilfeller (63,9 %).</li> </ul> </li> </ul> |

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|  |  |  |  |  | <div> <div>- Fremføring: 35 antegrad (15,3 %), 194 retrograd (84,7 %).</div> <div> <div>• Primære endepunkter:</div> <div> <div>- Kombinert sikkerhetsendepunkt (fravær av større komplikasjoner på tilgangsstedet innen 6 timer etter prosedyren) og effektendepunkt (vellykket hemostase på punksjonsstedet) ble oppnådd i 215/226 (95,1 %) [95 % KI: 91,46; 97,55] pasienter i det fullstendige analysesettet og 215/230 (93,5 %) [95 % KI 89,47, 96,30] i sett behandlet med FemoSeal™.</div> <div>- Effektendepunktet ble oppnådd hos 219/226 (96,9 %) CI [93,7, 98,7] pasienter.</div> <div>- Sikkerhetsenedepunkt oppnådd i 220/230 (95,2 %) [95 % CK: 92,15, 97,90] pasienter.</div> </div> </div> <div> <div>• Sekundære endepunkter:</div> <div> <div>- Fravær av mindre komplikasjoner på tilgangsstedet i seks timer etter prosedyren ble oppnådd i 225/230 (97,8 %) [95 % KI: 95,00; 99,29].</div> <div>- Fravær av større og mindre komplikasjoner på tilgangsstedet fra seks timer til 30 dager etter prosedyren ble oppnådd hos 219/230 (95,2 %) [95 % KI: 91,60; 97,59] pasienter.</div> <div>- Mediantid til hemostase med FemoSeal™ VCD: 0,42 (0,25; 0,50) minutter.</div> </div> </div> </div> |
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|--|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <ul style="list-style-type: none"> <li>- Mediantid til ambulerings: 5,00 (4,54; 5,50) minutter.</li> <li>- Medianvarighet for sykehusopphold: 23,98 (22,72, 25,00) timer.</li> <li>- Brukervennlighet for FemoSeal™ VCS: «enkel» eller «svært enkel» å sette inn i 98,7 % av tilfellene («enkel» å sette inn i 21 (9,2 %), «svært enkel» å sette inn i 205 (89,5 %) med ingen eller lav motstand ved innsetting i 226 (98,3 %) tilfeller.</li> </ul> <p>152/230 (66,1 %) av pasientene ble behandlet med guidewiren som er inkludert i FemoSeal™-settet (GW 0,038") og anbefalt i FemoSeal™ uten rapporterte utstyrsfeil eller bivirkninger.</p> |
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2006-studien ble utført for å bekrefte sikkerheten og effektiviteten til den nåværende enheten med et forbedret innføringssystem og for å få tilbakemeldinger om FemoSeal™ VCS IFU og opplæringsprogrammet. Studien inkluderte 100 pasienter, og det primære slutt punktet var om hemostase ble oppnådd, eller om ytterligere manuell eller mekanisk kompresjon var nødvendig. Denne studien konkluderte med at bruk av FemoSeal™ VCS var vellykket i de fleste tilfellene (91% oppnådde umiddelbar hemostase).

Studien i 2008 inkluderte 50 pasienter for å vurdere sikkerheten og ytelsen til FemoSeal™ VCS ved bruk under normal klinisk rutine hos pasienter som fikk utført kardial kateterisering med en 7 Fr-hylse. Studiens primære slutt punkt var å samle inn data om tid til hemostase og tid til ambulerings uten ytterligere kompresjon, manuell eller mekanisk. Studieresultatene konkluderte med at gjennomsnittlig tid til hemostase var 57,8 sekunder, og at alle pasienter var ambulering etter 4 timer med hvile.

2009-studien var ment å evaluere den nye FemoSeal™ VCS-emballasjen. 25 pasienter var inkludert i studien. Det primære endepunktet var om brukeren opplevde problemer med emballasjen. Brukerne merket ingen problemer med den nye FemoSeal™ VCS-emballasjen. Denne studien samlet også inn data for tid til hemostase.

Formålet med 2022-studien var proaktiv innsamling av data om sikkerheten og effekten til FemoSeal VCS gjennom oppnådd hemostase i tilgangsstedet for hovedlårarterien hos reelle

forsøkspersoner som gjennomgår perkutane endovaskulære prosedyrer. 230 pasienter var inkludert i studien. Primære endepunkter for registeret er prosedyremessig suksess (dvs. vellykket hemostase på punksjonsstedet) og reduksjon i alvorlige komplikasjoner (f.eks. vaskulær skade, blødning relatert til tilgangsstedet, infeksjon på tilgangsstedet, gjentatt manuell kompresjon og ny tilgangsstedrelatert ipsilateral akutt iskemi i bena). Studien konkluderte med at FemoSeal™ VCS fungerer godt i reelle omgivelser og gir effektiv hemostase og lav forekomst av komplikasjoner på tilgangsstedet for pasienter som gjennomgår perifere endovaskulære intervensjoner. Det viser god ytelse med kort tid til hemostase og god brukertilbakemelding, noe som gjør FemoSeal™ VCS til en verdifull enhet for lukking av femoral tilgang.

### 1.4.3 Oppsummering av data fra klinisk oppfølging etter markedsføring

#### 1.4.3.1 Fullførte kliniske studier etter markedsføring

Et sammendrag av de fullførte kliniske oppfølgingsaktivitetene etter markedsføring er beskrevet i **tabell 1.7** nedenfor.

**Tabell 1.7. Kliniske oppfølgingsaktiviteter etter markedsføring**

| Fullførte kliniske oppfølgingsaktiviteter etter markedsføring             |             |                                                                         |                                                                                                                                                                    |                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|---------------------------------------------------------------------------|-------------|-------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Navn på aktivitet                                                         | År/CI       | Type studie                                                             | Målsetninger                                                                                                                                                       | Milepæler                                                                                                                                                          | Potensielle akseptkriterier                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021<br>TMC | Klinisk undersøkelse etter markedsføring – undersøkelse av høy kvalitet | Undersøkelse etter markedsføring for å samle inn prospektive tilbakemeldinger relatert til bruken av FemoSeal™ Vascular Closure Device distribuert i EU-markedene. | <ul style="list-style-type: none"> <li>120 tilfeller</li> <li>8 individuelle leger med mer enn 5 års erfaring</li> <li>Flere land i Europa</li> </ul>              | <b>Skalaevalueringer av enheten fra 1–5 – Uttalelser fra undersøkelsen</b> <ul style="list-style-type: none"> <li>Akseptkriterier               <ul style="list-style-type: none"> <li>Rangeringer på 3–5 anses som gunstige</li> <li>Alle uttalelser bør ha ≥ 80 % positiv tilbakemelding</li> </ul> </li> <li>Resultater               <ul style="list-style-type: none"> <li>Ingen svar fra undersøkelsen mottok &gt; 20 % ugunstige svar</li> <li>Det ble ikke rapportert klager på produktet</li> </ul> </li> </ul> |
| 20210298 – 0.035” and 0038” Guidewire Clinical Survey                     | 2021<br>TMC | Klinisk undersøkelse etter markedsføring –                              | Undersøkelse etter markedsføring for å samle inn prospektive tilbakemeldinger                                                                                      | <ul style="list-style-type: none"> <li>Undersøkelser for 0,035" wire               <ul style="list-style-type: none"> <li>106 undersøkelser</li> </ul> </li> </ul> | <b>Skalaevalueringer av enheten fra 1–5 – Uttalelser fra undersøkelsen</b> <ul style="list-style-type: none"> <li>Akseptkriterier</li> </ul>                                                                                                                                                                                                                                                                                                                                                                             |

| Fullførte kliniske oppfølgingsaktiviteter etter markedsføring                                                                   |                         |                                                                         |                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|---------------------------------------------------------------------------------------------------------------------------------|-------------------------|-------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Report (2021)                                                                                                                   |                         | undersøkelse av høy kvalitet                                            | relatert til bruken av 0,035" guidewire som følger med 6 Fr Angio-Seal™ VIP Vascular Closure Device (VCD) og 0,038" som følger med både 8 Fr Angio-Seal™ VIP VCD og FemoSeal Vascular Closure System distribuert i EU-markedene. | <ul style="list-style-type: none"> <li>○ 64 leger</li> <li>• Undersøkelser for 0,038" wire <ul style="list-style-type: none"> <li>○ 109 undersøkelser</li> </ul> </li> <li>○ 55 leger</li> <li>• 12 retrospektive undersøkelser</li> </ul>                                                                                                                              | <ul style="list-style-type: none"> <li>○ Rangeringer på 3–5 anses som gunstige</li> <li>○ Alle uttalelser bør ha <math>\geq 80\%</math> positiv tilbakemelding</li> <li>• Resultater <ul style="list-style-type: none"> <li>○ Alle guidewirer fikk akseptable vurderinger</li> <li>○ Det ble ikke rapportert klager på produktet</li> </ul> </li> </ul>                                                                                                                                                                                                                                                                                                                                                    |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024<br><br>TMC/TE | Klinisk undersøkelse etter markedsføring – undersøkelse av høy kvalitet | Prospektiv innsamling av tilbakemeldinger knyttet til bruken av FemoSeal VCS med guidewirer distribuert i EU-markedet.                                                                                                           | <ul style="list-style-type: none"> <li>• 126 undersøkelser <ul style="list-style-type: none"> <li>• 7 steder</li> <li>• 5 land</li> </ul> </li> <li>• 14. november 2023–11. juni 2024</li> <li>• Legenes medisinske spesialitet: <ul style="list-style-type: none"> <li>○ Vaskulær kirurg</li> <li>○ Intervensjons radiolog</li> <li>○ Angiologi</li> </ul> </li> </ul> | <b>Evalueringer av enheten på en skala til 5 – Uttalelser fra undersøkelsen</b> <ul style="list-style-type: none"> <li>• Akseptkriterier <ul style="list-style-type: none"> <li>○ Rangeringer på 3–5 anses som gunstige</li> <li>○ Alle uttalelser bør ha <math>\geq 80\%</math> positiv tilbakemelding</li> <li>○ Hvis det oppstår bivirkninger i denne undersøkelsen, skal de være bivirkninger som er forventet i risikostyringen.</li> </ul> </li> <li>• Pasientdemografi <ul style="list-style-type: none"> <li>○ Kvinner: 29,4 % (37/126)</li> <li>○ Menn: 69,8 % (88/126)</li> <li>○ Kjønn ikke angitt: 0,8 (1/126)</li> <li>○ Alder &gt;75 år: 31,7 %</li> </ul> </li> <li>• Resultater</li> </ul> |

| Fullførte kliniske oppfølgingsaktiviteter etter markedsføring |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|---------------------------------------------------------------|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                               |  |  |  |  | <ul style="list-style-type: none"> <li>○ Guidewire som følger med FemoSeal™ VCS: 101/126 (80,2 %).</li> <li>○ Prosedyrevarighet (minutter): 63,4 (36,6) (middelerdi (SD)); 57,0 (36,0-81,0) (medianverdi (IQR))</li> <li>○ Alle vurderinger av ytelsen til FemoSeal™ VCS var gunstige.</li> <li>○ Alle vurderinger av guidewiren som følger med FemoSeal™ VCS, var gunstige.</li> <li>○ Én (0,8 %) bivirkning: FemoSeal™ VCS-skivene var ikke godt innrettet, sannsynligvis på grunn av bruk av en stiv guidewire (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 tommer) som krevde manuell kompresjon for å oppnå hemostase.</li> </ul> |

Terumo Medical Corporation har fullført tre brukerundersøkelser av høy kvalitet blant leger i løpet av gjeldende rapporteringsperiode (01. september 2019-31. august 2024).

Kliniske undersøkelser om FemoSeal™ samlet proaktive kliniske data i forbindelse med sikkerheten og ytelsen til FemoSeal™ VCS under klinisk bruk. Undersøkelsen omfattet spørsmål med fokus på enheten generelt og tilknyttet tilbehør, inkludert guidewiren på 0,038 tommer og den direkte interaksjonen mellom dem. De kliniske undersøkelsene av guidewiren samlet inn proaktive kliniske data i forbindelse med sikkerhet og ytelse under klinisk bruk av guidewiren på 0,038 tommer som leveres med FemoSeal™ VCS. Spørsmålene i undersøkelsen fokuserte spesifikt på generell bruk av guidewiren, fra innføring gjennom prosedyrehylsen inn i vaskulaturen til og med fjerning av wiren.

FemoSeal™ VCS og guidewiren på 0.038" som fulgte med utstyret, fikk akseptable vurderinger, og det ble registrert seks (6) klager på enheten og ni (9) anmerkninger for guidewiren basert på evaluering av kommentarene fra de kliniske kvalitetsundersøkelsene. Reklamasjonene er evaluert for både FemoSeal og guidewiren, og ble vurdert som en del av Terumos overvåkingsprosjekt etter markedsføring. Ingen nye risikoer og/eller risikonivåer ble identifisert.

En brukerundersøkelse blant leger ble gjennomført i 2024 som en del av PMCF-aktivitetene. Resultatene av undersøkelsen viste at ytelsesvurderingen og sikkerheten til FemoSeal™ VCS generelt var svært gunstig. Kompatibiliteten til andre guidewirer enn den som følger med FemoSeal™ VCS som standard, ble også vist.

#### **1.4.3.2 Løpende/planlagt klinisk oppfølging etter markeds lansering**

TMC har én pågående/planlagt klinisk oppfølgingsaktivitet etter markedsføring. Det vil bli utført en klinisk undersøkelse for å innhente tilbakemeldinger relatert til bruk av guidewiren med FemoSeal VCS distribuert på EU-markedet. Undersøkelsen vil bli besvart av leger for å studere hvilke guidewirer de brukte under prosedyren. Hensikten med denne undersøkelsen er å adressere et gap identifisert som mangel på litteratur og kommentarer fra eksterne granskere om hvor kompatibel FemoSeal™ VCS er med bruk av andre guidewirer fra andre merker enn Terumo. Tilbakemeldingen omfatter tekniske resultater, klinisk ytelse og sikkerhet knyttet til utstyrets ytelse med ulike guidewirer.

#### **1.4.4 Sammendrag av data fra systematisk litteraturgjennomgang**

Terumo Medical Corporation gjennomfører systematiske litteraturgjennomganger for å samle inn og evaluere kliniske sikkerhets- og ytelsesdata fra publiserte studier om FemoSeal™ VCS og/eller lignende utstyr. Målet med den årlige screeningen av publisert litteratur er å identifisere tidligere ukjente bivirkninger, overvåke kjente bivirkninger, identifisere oppståtte risikoer og identifisere mulig systematisk feilbruk eller ikke-godkjent bruk av FemoSeal™ VCS.



Den siste systematiske litteraturgjennomgangen, som omfattet perioden fra 1. september 2019 til og med 31. august 2024, identifiserte 29 publiserte studier som ga data om klinisk sikkerhet og ytelse for FemoSeal™ VCS. 23 referanser rapporterte bruk av FemoSeal™ VCS i henhold til anvisningene (on-label), og bruk som ikke var i henhold til anvisningene (off-label) ble rapportert i ni studier. Litteraturgjennomgangen av studier som er spesifikke for bruk av FemoSeal™ VCS, viser samlet sett en populasjon under studie som er representativ for pasienter i EU som gjennomgår perkutane vaskulære kateteriseringsprosedyrer. Se listen over disse 23 fagfellevurderte publikasjonene i **Avsnitt 3**.

Klinisk ytelse ble vurdert ved følgende måleverdier:

- Tiden til hemostase er bedre enn eller sammenlignbar med dagens tekniske status for perkutan lukking av lårarterien.
- Tiden til ambulering er bedre enn eller sammenlignbar med dagens tekniske status for perkutan lukking av lårarterien.
- Forekomsten av postoperative komplikasjoner er sammenlignbar med eller lavere enn dagens tekniske status.

Basert på disse målingene av klinisk ytelse, viste dataene i denne litteraturgjennomgangen at FemoSeal™ VCS kan brukes til å lukke punksjon i lårarterien (arteriotomi) hos pasienter som har gjennomgått perkutan kateterisering med en kirurgisk hylse på 7°Fr eller mindre. Fullstendig hemostase ble oppnådd hos de fleste pasientene (79,65–100 %), og var forbundet med en mediantid til hemostase på 0,5 min, og mediantid til utskriving var 3 dager. Mellom 69,2-86,7 % av pasientene var i stand til å bevege seg 5 timer etter lukking, med et gjennomsnittlig postoperativ sengeleie på 349 min. Svikt i FemoSeal™ VCS ble observert i 3,68-4 % av tilfellene, og ytterligere manuell kompresjon var nødvendig i 0,9-4,4 % av prosedyrene.

Klinisk sikkerhet ble vurdert ved bivirkninger, inkludert, men ikke begrenset til:

- Blødning
- Hematom
- Pseudoaneurisme
- Blåmerke
- Arteriovenøs fistel
- Infeksjon
- Død

For hver av disse bivirkningene var forekomstraten som ble rapportert for FemoSeal™ VCS i de inkluderte studiene, mindre enn eller sammenlignbar med historisk rapporterte rater for manuell kompresjon og andre vaskulære lukkeinnetninger.

Ingen bivirkninger ble identifisert ved gjennomgang av 10 kasusrapporter, siden ingen nye, uventede, nye eller uakseptable risikoer ble identifisert.

Den generelle effektiviteten ved bruk av FemoSeal™ VCS under diagnostisk angiografi eller intervensjonelle operasjoner avhenger av flere faktorer, som kjønn, alder, pasientens anatomi, komorbiditeter, anatomisk plassering av punksjonsstedet, kirurgens erfaring, VCD-plasseringsmetode, postoperativ pleie osv. I tillegg til teknisk suksess, inkludert oppnåelse av hemostase, ga FemoSeal™ VCS kliniske fordeler med tanke på vaskulær lukking etter punktering av lårarterien, som redusert tid til hemostase, redusert tid til ambulering. Ytelsesresultatene for FemoSeal VCS™ er i samsvar med de som forventes for denne typen enhet når den brukes som tiltenkt. Noen av referansene som ble innhentet i løpet av den gjeldende søkeperioden, viste bruk av den undersøkte enheten på et annet anatomisk sted enn lårarterien og for lukking av arteriotomier > 7 Fr, noe som anses ikke å være i henhold til anvisningene (off-label).

Ingen ukjente bivirkninger, nye risikoer eller mulig systematisk feilbruk av enheten ble identifisert under gjennomgangen. Hvis FemoSeal™ VCS imidlertid brukes med forsiktighet av opplærte leger, fungerer det medisinske utstyret som et nyttig og nødvendig klinisk utstyr. Samlet sett løser målbehandlingen og dermed FemoSeal™ VCS det kliniske behovet som for tiden eksisterer ved behandling av komplikasjoner knyttet til vaskulær tilgang.

Dataene i denne litteraturgjennomgangen identifiserte samlet sett ingen tidligere ukjente ytelses- eller sikkerhetsproblemer i klinikk, eller bivirkninger som forekom ved høyere enn forventede/akseptable rater. Derfor kan det konkluderes fra denne litteraturen at FemoSeal™ VCS, når den brukes til å gi kompresjon for hemostase ved arteriotomien etter perkutan kateterisering, fortsetter å fungere som forventet og ikke er forbundet med alvorlige sikkerhetshendelser.

#### **1.4.5 Oppsummering av data fra kliniske studier etter markedsføring**

Et proaktivt PMS-system er på plass, og en gjennomgang av alle klager fullføres månedlig og i samsvar med interne produksjonsprosedyrer. Reklamasjonsdata ble analysert i tidsrommet 1. september 2019 til 31. august 2024. Totalt ble 28 rapporter om medisinsk utstyr og 476 rapporter om kundeklager sendt til produsenten. Av de 28 rapportene om medisinsk utstyr var 27 forbundet med bivirkninger og én forbundet med funksjonsfeil på enheten. Det var to dødsfall i løpet av rapporteringsperioden, men ingen av de rapporterte dødsfallene ble vurdert å være forbundet med studieenheten. Av de 476 klagenes som ble sendt til produsenten, var de vanligste årsakene til klagenes vanskeligheter ved plassering (146 forekomster, 0,0142 % forekomstrate). Hendelser med feilmodus ved uttrekking er den nest hyppigste med en frekvens på 0,0126 % (130 hendelser).

Det er solgt mer enn 1 030 136 FemoSeal™ Vascular Closure System-enheter globalt, og 827 843 i det europeiske økonomiske samarbeidsområdet. Den beregnede klagefrekvensen basert på globalt salg er 0,046 %. Den totale kundeklageraten er svært lav. Det ble ikke identifisert nye risikoer som ikke er inkludert i bruksanvisningen og risikodokumentasjonen.

Forekomsten av bivirkninger er vist i **Tabell 1.2**. Ingen nye uforutsette, nye eller uakseptable risikoer ble identifisert. Det var ingen signifikant økning i hyppighet eller alvorlighetsgrad av kjente bivirkninger.

#### 1.4.6 Generell oppsummering av klinisk ytelse og sikkerhet

FemoSeal™ VCS er indisert for bruk til lukking av punksjon i hovedlårarterien (arteriotomi) hos pasienter som har gjennomgått perkutan kateterisering med en kirurgisk hylse på 7F (2,33 mm) eller mindre. Denne kliniske evalueringen er basert på en omfattende analyse av tilgjengelige kliniske data og litteratur før og etter markedsføring som er relevante for tiltenkt bruk av FemoSeal™ VCS.

Det ble utført en omfattende gjennomgang av publisert litteratur i perioden fra 1. september 2019 til og med 31. august 2024. Evidensmaterialet inkluderte 29 studier for FemoSeal™ VCS. Evidensmaterialet i den kliniske evalueringen konkluderer med at når den aktuelle enheten brukes som indisert, er den sikker og effektiv, og alle risikoer eller uønskede bivirkninger som kan være forbundet med enheten under normale bruksforhold, utgjør akseptable risikoer når de veies opp mot fordelene for pasienten. Ytelsesresultatene for de aktuelle enhetene er i samsvar med de som forventes for denne typen enhet når den brukes som tiltenkt.

De potensielle bivirkningene som er forbundet med bruk av FemoSeal™ VCS, omfatter vanlige bivirkningene som rapporteres med alternative metoder for lukking av arteriotomi, f.eks. blødning og hematom. Totalt sett er forekomsten av bivirkninger rapportert ved bruk av FemoSeal™ VCS lik hyppigheten rapportert for manuell kompresjon og lignende vaskulære lukkeinnetninger. Spesielt for blødning og hematom er de rapporterte hyppighetene for FemoSeal™ VCS mindre enn de rapporterte hyppighetene for lignende vaskulært lukkeutstyr. Hver av de rapporterte bivirkningene fra både publisert litteratur og overvåking etter markedsføring, var tidligere identifisert (se **avsnitt 1.3**).

De eksisterende dataene vedrørende den kliniske sikkerheten og ytelsen til FemoSeal™ VCS tyder på at pasienten drar nytte av at bruken av denne vaskulære lukkeenheten oppveier mulige risikoer når den brukes i samsvar med bruksanvisningen.

Som angitt i avsnittene ovenfor, viser tilgjengelige data for FemoSeal™ VCS konsistens mellom dataene som er relatert til enheten som evalueres (f.eks. bruk av enheten, sikkerhetsresultater, klinisk ytelse og klinisk nytte), identifiserte tilsvarende enheter og data relatert til lignende enheter i henhold til den nyeste litteraturen.

Kryssanalysen av sikkerhetsdata identifiserte ingen avvik mellom:

- Data som er nevnt i den nyeste litteraturen
- Data som er spesifikke for enheten som evalueres
- Data nevnt i risikohåndteringsfilen(e)

- Data som er nevnt i merkingen og/eller bruksanvisningen (dvs. restrisikoer som overføres til brukeren er adressert).

Klinisk sikkerhet er vist ved lave forekomster av komplikasjoner identifisert i publisert, fagfellekvurdert klinisk litteratur, selskapssponsede kliniske studier, gjennomgang av data etter markedsføring kombinert med ingen tilbaketrekninger fra markedet. Det er ikke identifisert noen bekymringer med tanke på ytelse. Litteraturen som ble gjennomgått, inneholdt bruk av FemoSeal™ VCS som var i samsvar med produsentens tiltenkte bruk.

### 1.5 Mulige diagnostiske eller terapeutiske alternativer

Manuell kompresjon brukes tradisjonelt til å oppnå hemostase på arteriotomistedet etter vaskulær kateterisering. Manuell kompresjon har vært forbundet med langvarig immobilisering av pasienten (opptil 8 timer etter en prosedyre), samt med betydelig ubehag og lengre sykehusopphold. En nylig systematisk gjennomgang fant at mediantid til hemostase med manuell kompresjon var 20,8 minutter.<sup>1</sup>

Alternativer til manuell kompresjon omfatter eksterne hemostatisk enheter som påfører mekanisk kompresjon på arteriotomistedet. Disse enhetene reduserer ikke tiden til hemostase eller tiden til ambulerende, men reduserer personalbehovet ved å erstatte manuell kompresjon med mekanisk kompresjon. Bivirkningshyppighet forbundet med bruk av mekanisk kompresjon ligner hyppigheten ved manuell kompresjon.

Vaskulært lukkeutstyr, som FemoSeal™ VCS, er designet for å lukke arteriotomien. Formålet med utstyret er å redusere tiden til hemostase og muliggjøre tidligere ambulerende. En nylig systematisk gjennomgang, inkludert 13 kommersielt tilgjengelige enheter, fant at mediantid til oppnå hemostase med et vaskulært lukkesystem var 5,4 minutter. Mediantid til hemostase for de individuelle vaskulære lukkeenhetene var fra 1 minutt (FemoSeal™ VCS) til 14 minutter, og var mellom 4 og 10 minutter for flertallet av enhetene.<sup>1</sup>

Vanlig rapporterte bivirkninger forbundet med lukking av arteriotomistedet med manuelle kompresjoner, eksternt hemostatisk utstyr eller vaskulært lukkeutstyr inkluderer hematom, blødning på tilgangsstedet, pseudoaneurisme, arteriovenøs fistel og infeksjon. Den samme systematiske gjennomgangen (34 randomiserte kontrollerte studier, 14 401 pasienter) fant at bivirkningsratene var lignende mellom manuell kompresjon og bruk av vaskulære lukkeanordninger, med unntak av at blødningene hadde en tendens til å være litt høyere med vaskulære lukkeanordninger.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Foreslått brukerprofil og opplæring

Tiltenkte brukere av FemoSeal™ Vascular Closure System er leger med opplæring som kvalifiserer dem til å utføre arteriell tilgang og lukking for endovaskulære prosedyrer gjennom hovedlårarterien, og som har deltatt i et legeinstruksjonsprogram for Terumo Medical Corporation FemoSeal™.

## 1.7 Relevante harmoniserte og felles standarder

| Referansestandard | Gjeldende samsvarsår/rev. | Beskrivelse                                                                                                                              |
|-------------------|---------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070         | 2014/AMD1:2018            | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070      | 2014/A1:2018              | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance      | 20. mai 2021              | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052        | 2015                      | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213        | 2017                      | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503        | 2020                      | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182        | 2019                      | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |
| EN ISO 13485      | 2016/A11:2021             | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 13485         | 2016                      | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |

| Referansestandard | Gjeldende samsvarsår/rev. | Beskrivelse                                                                                                                                                              |
|-------------------|---------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14644-1       | 2015                      | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1    | 2015                      | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2       | 2015                      | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2    | 2015                      | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3       | 2019                      | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3    | 2019                      | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1       | 2003                      | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1    | 2003                      | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2       | 2003/TC1:2004             | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| EN ISO 14698-2    | 2003/TC 1:2004            | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| USP <788>         | N/A                       | PARTICULATE MATTER IN INJECTIONS                                                                                                                                         |

| Referansestandard   | Gjeldende samsvarsår/rev. | Beskrivelse                                                                                                          |
|---------------------|---------------------------|----------------------------------------------------------------------------------------------------------------------|
| EU-farmakopé 2.9.19 | N/A                       | Particulate Contamination: Sub-Visible Particles                                                                     |
| IEC 62366-1         | 2015                      | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN 62366-1          | 2015                      | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN ISO 14971        | 2019/A11:2021             | Medical devices — Application of risk management to Medical devices                                                  |
| ISO 14971           | 2019                      | Medical devices — Application of risk management to Medical devices                                                  |
| ASTM F1980          | 2016                      | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1      | 2020                      | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1         | 2018                      | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2      | 2006                      | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2         | 2006                      | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3      | 2014                      | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3         | 2014                      | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4      | 2017                      | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4         | 2017                      | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |



| Referansestandard | Gjeldende samsvarsår/rev. | Beskrivelse                                                                                                                                |
|-------------------|---------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-5    | 2009                      | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                                         |
| ISO 10993-5       | 2009                      | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                                         |
| EN ISO 10993-6    | 2016                      | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| ISO 10993-6       | 2016                      | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| EN ISO 10993-10   | 2023                      | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| ISO 10993-10      | 2021                      | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| EN ISO 10993-11   | 2018                      | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| ISO 10993-11      | 2017                      | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| EN ISO 10993-12   | 2021                      | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| ISO 10993-12      | 2021                      | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| EN ISO 10993-17   | 2009                      | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17      | 2002                      | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18      | 2020/A1:2022              | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |



| Referansestandard | Gjeldende samsvarsår/rev. | Beskrivelse                                                                                                                                                                  |
|-------------------|---------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-18   | 2020/A1:2022              | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-23   | 2021                      | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23      | 2021                      | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382        | 2018                      | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756         | 2017                      | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>          | N/A                       | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>         | N/A                       | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72    | 2019                      | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135      | 2014/A1:2019              | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135         | 2014/A1:2018              | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7    | 2008/A1:2022              | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |

| Referansestandard | Gjeldende samsvarsår/rev. | Beskrivelse                                                                                                                                                     |
|-------------------|---------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-7       | 2008/A1:2019              | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                               |
| EN 556-1          | 2024                      | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices |
| EN ISO 11737-1    | 2018/A1:2021              | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11737-1       | 2018/A1:2021              | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| EN ISO 11138-1    | 2017                      | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-1       | 2017                      | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| EN ISO 11138-2    | 2017                      | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 11138-2       | 2017                      | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| EN ISO 15223-1    | 2016                      | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| ISO 15223-1       | 2016                      | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| EN 1041           | 2008/A1:2013              | Information supplied by the manufacturer of medical devices                                                                                                     |
| EN ISO 11607-1    | 2020/A1:2023              | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                         |

| Referansestandard | Gjeldende samsvarsår/rev. | Beskrivelse                                                                                                                                                                |
|-------------------|---------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11607-1       | 2019/A1:2023              | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| EN ISO 11607-2    | 2020/A1:2023              | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ISO 11607-2       | 2019/A1:2023              | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169        | 2016                      | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M | 2016                      | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825        | 2018                      | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096        | [2011 R 2019)             | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M     | 2015                      | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24      | 2021                      | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3       | 2020                      | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |
| MDCG 2020-8       | 2020                      | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                             |
| MDCG 2020-7       | 2020                      | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                          |

| Referansestandard | Gjeldende samsvarsår/rev. | Beskrivelse                                                                                                                                                                                                                                                   |
|-------------------|---------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-6       | 2020                      | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                                                                                                          |
| MDCG 2019-9 v1    | 2022                      | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                                                                                      |
| MDCG 2019-8 v2    | 2020                      | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15      | 2020                      | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11      | 2021                      | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19      | 2021                      | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4    | 2021                      | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2       | 2019                      | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1       | 2019                      | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7       | 2018                      | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6       | 2018                      | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |

| Referansestandard   | Gjeldende samsvarsår/rev. | Beskrivelse                                                                                                                                                                                   |
|---------------------|---------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2018-4         | 2018                      | MDCG 2018-4 Annex: UDI database<br>Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                               |
| MDCG 2018-3 v1      | 2020                      | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25        | 2021                      | Regulation (EU) 2017/745 - application of MDR requirements to ‘legacy devices’ and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2.12-2 Rev 2 | 2012                      | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                        |

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### 3.0 ENDRINGSHISTORIKK

| SSCP-revisjonsnummer      | Utstedt dato    | Endringsbeskrivelse                                                  | Revisjon validert av teknisk kontrollorgan                                                                                                                                                                                                                                                                                 |
|---------------------------|-----------------|----------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022              | 20. januar 2023 | Første utgave, etter MDR CE-sertifisering                            | <p><input checked="" type="checkbox"/> Ja</p> <p>Valideringsspråk: English</p> <p><input type="checkbox"/> Nei (gjelder kun for klasse IIa eller noen klasse IIb implanterbare enheter (MDR, artikkel 52 (4) 2. avsnitt) som SSCP ennå ikke er validert for av NB)</p> <p><input type="checkbox"/> Annet (spesifiser):</p> |
| SSCP-FS-2023 – Revisjon 1 | 15. mars 2024   | Oppdatert for perioden 1. januar 2019 til og med 31. desember 2023.  | <p><input checked="" type="checkbox"/> Ja</p> <p>Valideringsspråk: English</p> <p><input type="checkbox"/> Nei (gjelder kun for klasse IIa og noen klasse IIb implanterbare enheter (MDR, artikkel 52 (4) 2. avsnitt) som SSCP ennå ikke er validert for av NB)</p> <p><input type="checkbox"/> Annet (spesifiser):</p>    |
| SSCP-FS-2024 Revisjon 1   |                 | Oppdatert for perioden 1. september 2019 til og med 31. august 2024. | <p><input type="checkbox"/> Ja</p> <p>Valideringsspråk: English</p> <p><input type="checkbox"/> Nei (gjelder kun for klasse IIa og noen klasse IIb implanterbare enheter (MDR, artikkel 52 (4) 2. avsnitt) som SSCP ennå ikke er validert for av NB)</p> <p><input type="checkbox"/> Annet (spesifiser):</p>               |

|                            |               |                                                       |                                                                                                                                                                                                                                                                                                                                                             |
|----------------------------|---------------|-------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>Revisjon 2 | June 20, 2025 | Revidert basert på<br>NSAI-spørsmål til<br>validering | <div><input checked="" type="checkbox"/> Ja</div> <div>Valideringsspråk: English</div> <div><input type="checkbox"/> Nei (gjelder kun for klasse<br/>IIa og noen klasse IIb<br/>implanterbare enheter (MDR,<br/>artikkel 52 (4) 2. avsnitt) som<br/>SSCP ennå ikke er validert for<br/>av NB)</div> <div><input type="checkbox"/> Annet (spesifiser):</div> |
|----------------------------|---------------|-------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

## Podsumowanie bezpieczeństwa i działania klinicznego

### FemoSeal™ Vascular Closure System

|                                                            |                                                                                            |
|------------------------------------------------------------|--------------------------------------------------------------------------------------------|
| <b>Wytwórca</b>                                            | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 USA        |
| <b>SRN producenta</b>                                      | US-MF-000019594                                                                            |
| <b>Przedstawiciel kierownictwa/PRRC</b>                    | Kimberly Feitl<br>Vice President, Quality                                                  |
| <b>Podstawowe UDI-DI</b>                                   | 38970FS79                                                                                  |
| <b>Numer EMDN</b>                                          | C900199 — Systemy hemostatyczne — Inne                                                     |
| <b>Klasa wyrobu</b>                                        | Klasa III                                                                                  |
| <b>Rok, w którym wyrób uzyskał znak CE po raz pierwszy</b> | 2005                                                                                       |
| <b>Przedstawiciel EC</b>                                   | Terumo Europe N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgia<br>SRN: BE-AR-000001433 |
| <b>Jednostka notyfikowana</b>                              | NSAI<br>CE 0050                                                                            |

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Niniejsze podsumowanie bezpieczeństwa i działania klinicznego (SSCP) ma na celu zapewnienie publicznego dostępu do aktualnego podsumowania głównych aspektów bezpieczeństwa i działania klinicznego wyrobu FemoSeal™ Vascular Closure System (VCS).

Poniżej w **części 1.0** znajduje się podsumowanie bezpieczeństwa i działania klinicznego wyrobu, przeznaczone dla użytkowników / pracowników ochrony zdrowia.

## **1.0 PODSUMOWANIE DLA UŻYTKOWNIKÓW / PRACOWNIKÓW OCHRONY ZDROWIA**

SSCP nie ma na celu zastąpienia instrukcji obsługi, która jest głównym dokumentem zapewniającym bezpieczne użytkowanie wyrobu, i nie zawiera porad diagnostycznych ani terapeutycznych dla przewidzianych użytkowników ani pacjentów. SSCP nie ma na celu zastąpienia obowiązkowych informacji na kartach implantu ani w innych obowiązkowych dokumentach.

### **1.1 Przeznaczenie wyrobu**

#### **1.1.1 Przeznaczenie**

FemoSeal™ Vascular Closure System jest wyrobem medycznym przeznaczonym do zamykania nakłucia tętniczego po przezskórnym cewnikowaniu przez tętnicę udową wspólną.

#### **1.1.2 Zastosowanie**

FemoSeal™ Vascular Closure System służy do zamykania nakłucia (arteriotomii) tętnicy udowej wspólnej u pacjentów, u których wykonano cewnikowanie przezskórne przy użyciu koszulki zabiegowej o średnicy 7F (2,33 mm) lub mniejszej.

#### **1.1.3 Przeciwwskazania i/lub ograniczenia**

FemoSeal™ Vascular Closure System jest przeciwwskazany u pacjentów z arteriotomią, w której używano koszulki lub urządzenia o rozmiarze większym niż 7F (2,33 mm).

#### **1.1.4 Docelowa populacja pacjentów**

Bezpieczeństwo i skuteczność wyrobu FemoSeal™ Vascular Closure System zostały ustalone u pacjentów w wieku 18 lat i starszych, którzy przeszli cewnikowanie przezskórne przy użyciu koszulki zabiegowej w rozmiarze 7F (2,33 mm) lub mniejszym.

#### **1.1.5 Specjalne grupy pacjentów**

Bezpieczeństwo i skuteczność wyrobu FemoSeal™ Vascular Closure System nie zostały ustalone w następujących populacjach pacjentów:

- Pacjenci ze współistniejącą chorobą autoimmunologiczną.
- Pacjenci poddawani zabiegowi trombolizy.
- Pacjenci z klinicznie istotną chorobą naczyń obwodowych.
- Pacjenci z niekontrolowanym nadciśnieniem (> 220 mmHg skurczowe lub > 110 mmHg rozkurczowe).

- Pacjenci z zaburzeniami krwawienia, w tym trombocytopenią (<100 000 płytek krwi) lub anemią (Hgb < 10 mg/dl).
- Pacjenci ze światłem tętnicy udowej wspólnej węższym niż 5 mm.
- Pacjenci z zaburzeniami czynności nerek i/lub wątroby.
- Pacjenci z innymi istotnymi chorobami współistniejącymi.
- Populacja o określonym pochodzeniu rasowym i/lub etnicznym.
- Pacjenci z zawałem mięśnia sercowego w ciągu poprzednich 72 godzin.
- Pacjenci z przeszczepem naczyniowym lub stentem w miejscu nakłucia.
- Pacjenci w ciąży lub karmiący piersią.
- Pacjenci w wieku poniżej 18 lat.

### 1.1.6 Przewidziani użytkownicy

Przewidzianymi użytkownikami wyrobu FemoSeal™ Vascular Closure System są lekarze przeszkoleni w zakresie uzyskiwania dostępu tętniczego i zamykania naczyń po zabiegach wewnątrznaczyniowych wykonywanych przez tętnicę udową wspólną, którzy ukończyli szkolenie lekarzy w zakresie obsługi systemu FemoSeal™ organizowane przez Terumo Medical Corporation.

## 1.2 Opis wyrobu

### 1.2.1 Opis wyrobu

Wyrób FemoSeal™ Vascular Closure System, produkowany przez Terumo Medical Corporation (TMC), to wchłanianalne urządzenie do zamykania naczyń krwionośnych, przeznaczone do uzyskiwania hemostazy tętnicy udowej po przezskórnym cewnikowaniu przez tętnicę udową wspólną.

Elementy zamykające systemu FemoSeal™ to dwa wchłanianalne krążki polimerowe, uszczelka wewnętrzna i zewnętrzny krążek blokujący, które są połączone wchłanianym multifilamentem i w ten sposób mechanicznie uszczelniają arteriotomię (patrz **ilustracja 1.1** i **ilustracja 1.2**). Po wsunięciu przez koszulkę ze stożkową obudową zewnętrzny krążek blokujący jest wbijany w multifilament, co powoduje mechaniczne zamknięcie miejsca wkłucia między wewnętrznym i zewnętrznym krążkiem blokującym. Uszczelka wewnętrzna i zewnętrzny krążek blokujący są utrzymywane na miejscu przez tarcie na multifilamencie. Hemostazę uzyskuje się za pomocą środków mechanicznych. Elementy zamykające ulegają degradacji w wyniku hydrolizy.

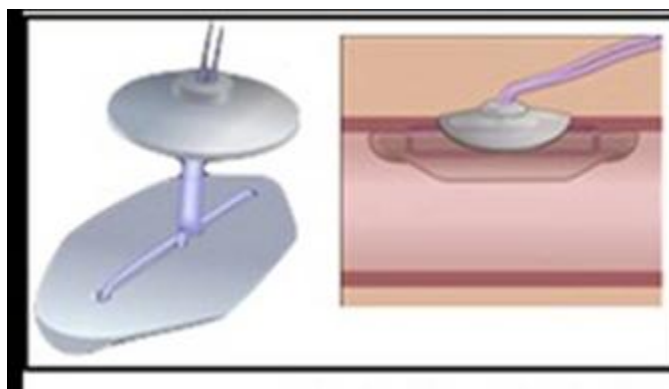


Wszezpialne elementy zamykajace, uszczelka wewnetrzna i zewnetrzny krążek blokujacy ulegaja rozkladowi w ciagu osiemnastu (18) miesiecy, podczas gdy multifilament ulega rozkladowi i jest wchlaniany w procesie hydrolizy przez otaczajaca tkanke po dwuch (2) do trzech (3) latach. Zdolnosc wszezpialnych elementow zamykajacych do utrzymania ucisku na arteriotomii zostala przetestowana w czasie do osmiu (8) godzin. Produkty rozkladu sa metabolizowane i wydane w moczu lub wydychane jako dwutlenek wegla przez pluca. W badaniach na zwierzetach nie zaobserwowano zjawiska akumulacji. Dodatkowe elementy systemu FemoSeal™, ktore beda mialy kontakt z zywa tkanka lub krwia podczas zabiegu, to koszulka ze stozkowa obudowa, rozszerzacz, ubijak, popychacz i przewodnik.

**Ilustracja 1.1 Uszczelka wewnetrzna i zewnetrzna tarcza ustalajaca, odpowiednio**

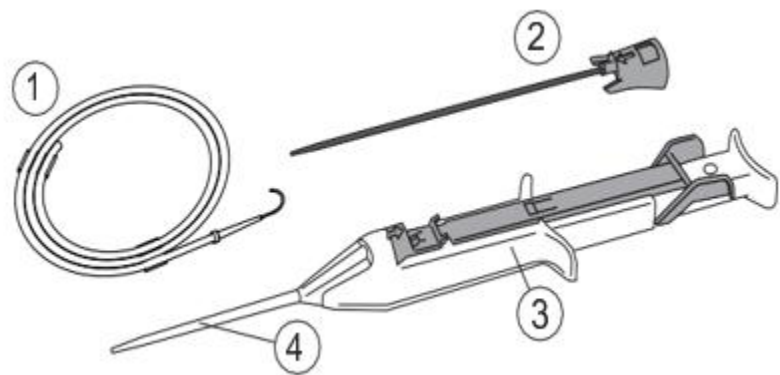


**Ilustracja 1.2 Uszczelka wewnetrzna i zewnetrzna tarcza ustalajaca, po wprowadzeniu**



System FemoSeal™ jest pakowany razem z rozszerzaczem i przewodnikiem o średnicy zewnętrznej 0,038" (0,97 mm), długości 27,5" (70 cm) i J-kształtnym manipulatorem, patrz **ilustracja 1.3** poniżej. Przewodnik znajduje się w rurce polietylenowej. Wszystkie części są zapakowane w przymocowaną papierową tacę. Opakowanie zawiera również kartę implantu dla pacjenta. Wyrób FemoSeal™ Vascular Closure System nie wymaga dodatkowych akcesoriów, aby urządzenie działać zgodnie z przeznaczeniem, i jest przeznaczony wyłącznie do stosowania z rozszerzaczem i przewodnikiem znajdującymi się w opakowaniu produktu.

Ilustracja 1.3 System FemoSeal™ VCS Unit z przewodnikiem i rozszerzaczem



1.2.2 Surowce i składniki

W tabeli 1.1 poniżej wymieniono elementy systemu FemoSeal™ VCS.

Tabela 1.1 Surowce i części systemu FemoSeal™ VCS

| Numer części | Opis                                                     |                                                                     | Materiały                                                                                                                                                                                           |
|--------------|----------------------------------------------------------|---------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1            | Przewodnik 0,038" (0,97 mm) z J-kształtnym manipulatorem |                                                                     | Przewodnik: Stal nierdzewna 304<br><br>J-kształtny manipulator: Polipropylen, fioletowy pigment<br><br>Zacisk: Polietylen<br><br>Dreny: Polietylen                                                  |
| 2            | Rozszerzacz FemoSeal                                     |                                                                     | Nasadka: Tetrahydrofuran, niebieski pigment, politereftalan butylenu (PBT)<br><br>Dren: Polietylen o dużej gęstości (HDPE), czarny pigment<br><br>Środek smarny: Silikonowy Dow Corning 360, heksan |
| 3/4          | System FemoSeal                                          | Formowane RD7 — uszczelka wewnętrzna i zewnętrzny krążek blokujący* | Kopolimer glikolidu, węglanu trimetylenu, ε-kaprolaktonu i TMP (trimetylolopropan (inicjator))                                                                                                      |
|              |                                                          | Multifilament *                                                     | Kopolimer segmentowany L,L-Laktydu, węglanu trimetylenu, ε-kaprolaktonu i propano-1,3-diolu (inicjator)<br><br>Powłoka jest kopolimerem glikolidu, ε-kaprolaktonu i L-lizyny                        |
|              |                                                          | Ubijak                                                              | Polipropylen                                                                                                                                                                                        |

|  |  |                              |                                                    |
|--|--|------------------------------|----------------------------------------------------|
|  |  | Popychacz                    | Stal nierdzewna 304V                               |
|  |  | Suwak                        | Politereftalan butylenu (PBT)                      |
|  |  | Obudowa                      | Politereftalan butylenu (PBT)                      |
|  |  | Przycisk                     | Politereftalan butylenu (PBT)                      |
|  |  | Pokrywa przycisku            | Polioksymetylen (POM)/kopolimer poliacetalowy      |
|  |  | Tuleja                       | Politereftalan butylenu (PBT)                      |
|  |  | Dystans                      | Politereftalan butylenu (PBT)                      |
|  |  | Stożek                       | Polipropylen                                       |
|  |  | Pokrywa obudowy              | Politereftalan butylenu (PBT)                      |
|  |  | Blokada bezpieczeństwa       | Politereftalan butylenu (PBT), niebieski pigment   |
|  |  | Pokrywa tulei                | Politereftalan butylenu (PBT)                      |
|  |  | Uszczelka rurki              | Silikonowy brzeg A 70                              |
|  |  | Uszczelka obudowy            | Silikonowy brzeg A 50                              |
|  |  | Sprężyna                     | Stal nierdzewna 302                                |
|  |  | Koszulka ze stożkową obudową | Polipropylen<br>Silikonowy Dow Corning 360, heksan |

\* Wszczepialna część wyrobu; wszczepialne elementy są bezpieczne w środowisku rezonansu magnetycznego

System FemoSeal™ VCS jest sterylizowany tlenkiem etylenu (EO) i jest wyrobem medycznym jednorazowego użytku. System FemoSeal™ VCS został zaprojektowany w taki sposób, że nie można go użyć ponownie.

### **Tryb pracy**

FemoSeal™ VCS wspomaga hemostazę mechaniczną, wprowadzając wszczepialne elementy zamykające wewnątrz i na zewnątrz tętnicy udowej wspólnej. Mechanizm zapobiegający krwawieniu składa się z dwóch części: uszczelki wewnętrznej, która zabezpiecza miejsce wkłucia, oraz zewnętrznego krążka blokującego, który utrzymuje uszczelkę wewnętrzną na miejscu.

### 1.2.3 Korzyści kliniczne

System FemoSeal™ VCS zapewnia następujące korzyści kliniczne w zakresie zamknięcia naczyn po nakłuciu tętnicy udowej wspólnej:

- Skrócenie czasu do hemostazy<sup>1</sup>
- Skrócenie czasu odzyskania sprawności ruchowej<sup>1</sup>

1. Cox, T., L. Blair, C. Huntington, A. Lincourt, R. Sing, i B.T. Heniford. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures*. *Surgical technology international*, 27, 32–44.

### 1.2.4 Poprzednie generacje lub warianty

- Pierwsza wersja systemu FemoSeal™ VCS (nr 11200) była sprzedawana na rynku europejskim w 2005 roku oraz przez część 2006 roku.
- Obecny system FemoSeal™ VCS (nr 11202), z ulepszonym systemem dostarczania, jest dostępny na rynku od 28 marca 2006 roku.

### 1.2.5 Akcesoria przeznaczone do użycia razem z urządzeniem

System FemoSeal™ jest pakowany razem z rozszerzaczem, przewodnikiem o średnicy zewnętrznej 0,038" (0,97 mm) i długości 27,5" (70 cm) oraz J-kształtnym manipulatorem. Prowadnik jest dodatkowym wyposażeniem systemu FemoSeal™. J-kształtny manipulator jest elementem przewodnika, podczas gdy rozszerzacz jest elementem systemu FemoSeal™. Prowadnik jest jedynym elementem dodatkowego wyposażenia. Prowadnik znajduje się w rurce polietylenowej. Wszystkie części są zapakowane w przymocowaną papierową tacę. Opakowanie zawiera również kartę implantu dla pacjenta. Wyrób FemoSeal™ Vascular Closure System nie wymaga dodatkowych akcesoriów, aby urządzenie działać zgodnie z przeznaczeniem, i jest przeznaczony wyłącznie do stosowania z rozszerzaczem i przewodnikiem znajdującymi się w opakowaniu produktu.

### 1.2.6 Inne urządzenia i produkty przeznaczone do użytku razem z urządzeniem

FemoSeal™ VCS nie wymaga dodatkowych urządzeń, aby działać zgodnie z przeznaczeniem.

## 1.3 Zagrożenia i ostrzeżenia

### 1.3.1 Ryzyko szczątkowe i niepożądane skutki

Znane lub możliwe do przewidzenia zdarzenia niepożądane, szkody i powikłania związane z użyciem systemu Angio-Seal™ VIP w wyniku ryzyka szczątkowego wymieniono w **tabeli 1.2**. Wskaźnik wystąpienia jest oparty na analizie dokumentacji ryzyka i obliczany na podstawie danych z monitoringu po wprowadzeniu na rynek od 1 września 2019 do 31 sierpnia 2024 r. Nie

ma nieznanych zagrożeń szczątkowych dla systemu FemoSeal™ VCS, a wszystkie stosowne zagrożenia zostały uwzględnione w instrukcji użytkowania i procesie zarządzania ryzykiem.

**Tabela 1.2. Zdarzenia niepożądane / Powikłania związane z FemoSeal**

| Szkoda                                             | Częstość występowania (%) | Czynniki łagodzące                                                                                                                                                                              |
|----------------------------------------------------|---------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Reakcja alergiczna                                 | 0,0000                    | Działania i plany mające na celu maksymalne zmniejszenie ryzyka zostały uwzględnione jako cechy konstrukcyjne produktu, wytyczne dotyczące produkcji, oznakowanie produktu i szkolenie lekarzy. |
| Tętniak                                            | 0,0000                    |                                                                                                                                                                                                 |
| Przetoka tętniczo-żylna                            | 0,0001                    |                                                                                                                                                                                                 |
| Utrata krwi / Krwawienie                           | 0,0280                    |                                                                                                                                                                                                 |
| Zgon                                               | 0,0002                    |                                                                                                                                                                                                 |
| Ekchymoza                                          | 0,0000                    |                                                                                                                                                                                                 |
| Zator                                              | 0,0000                    |                                                                                                                                                                                                 |
| Reakcja na ciało obce                              | 0,0000                    |                                                                                                                                                                                                 |
| Krwiak                                             | 0,0027                    |                                                                                                                                                                                                 |
| Krwotok                                            | 0,0001                    |                                                                                                                                                                                                 |
| Infekcja                                           | 0,0002                    |                                                                                                                                                                                                 |
| Reakcja zapalna                                    | 0,0000                    |                                                                                                                                                                                                 |
| Drętwienie                                         | 0,0000                    |                                                                                                                                                                                                 |
| Ból                                                | 0,0000                    |                                                                                                                                                                                                 |
| Dyskomfort pacjenta                                | 0,0004                    |                                                                                                                                                                                                 |
| Opóźnienie procedury                               | 0,0065                    |                                                                                                                                                                                                 |
| Tętniak rzekomy                                    | 0,0004                    |                                                                                                                                                                                                 |
| Krwawienie zaotrzewnowe                            | 0,0002                    |                                                                                                                                                                                                 |
| Sepsa                                              | 0,0000                    |                                                                                                                                                                                                 |
| Zator                                              | 0,0000                    |                                                                                                                                                                                                 |
| Zakrzepica żyły głębokiej                          | 0,0001                    |                                                                                                                                                                                                 |
| Niedrożność naczyń / Niedokrwienie kończyn dolnych | 0,0002                    |                                                                                                                                                                                                 |
| Perforacja naczynia                                | 0,0000                    |                                                                                                                                                                                                 |
| Rozwarstwienie/Rozerwanie tkanki naczynia          | 0,0003                    |                                                                                                                                                                                                 |

### 1.3.2 Ostrzeżenia i środki ostrożności

#### Ostrzeżenia

1. Nie używać, jeśli opakowanie zostało uszkodzone lub naruszono barierę sterylną.
2. Nie używać po upływie daty ważności — elementy biodegradowalne mogą nie działać prawidłowo.
3. Nie używać, jeśli któryś element wydaje się uszkodzony lub wadliwy.
4. Użycie wyrobu FemoSeal™ Vascular Closure System tam, gdzie mogło dojść do zakażenia bakteryjnego koszulki zabiegowej lub otaczającej tkanki, może spowodować zakażenie.
5. W razie podejrzenia, że tylna ściana tętnicy została nakłuta lub wykonano więcej niż jedno nakłucie tętnicy, nie należy polegać wyłącznie na wyrobie FemoSeal™ Vascular Closure System w celu uzyskania hemostazy tętnicy. Użyć dodatkowego ucisku manualnego lub mechanicznego.
6. Jeśli miejsce wkłucia znajduje się na rozgałęzieniu tętnicy udowej lub jest położone dystalnie względem tego rozgałęzienia, nie można używać wyrobu FemoSeal™ Vascular Closure System ze względu na ryzyko nieprawidłowego umieszczenia uszczelki wewnętrznej. To zdarzenie może spowodować powikłania krwotoczne i/lub zakłócenie normalnego przepływu krwi.
7. W przypadku utrzymującego się krwawienia tętniczego z miejsca nacięcia nie należy przecinać multifilamentu do czasu uzyskania hemostazy. Jeśli nie uda się uzyskać hemostazy, przymocować multifilament sterylnym opatrunkiem rany i zastosować dodatkowy ucisk do momentu uzyskania hemostazy. W przypadku utrzymującego się krwawienia tętniczego mogą wystąpić istotne powikłania krwawienia, które będą skutkować urazem lub śmiercią pacjenta.
8. Nie używać wyrobu FemoSeal™ Vascular Closure System, jeśli miejsce wkłucia jest położone proksymalnie względem więzadła pachwinowego, ponieważ może to spowodować krwiaka w przestrzeni zaotrzewnowej.
9. Pacjenci o podwyższonym ryzyku krwawienia mogą ucierpieć z powodu utraty dużej ilości krwi i będą wymagać transfuzji.
10. Jeśli wewnętrzny krążek odłączy się, może spowodować zakrzep i/lub embolizm.

#### Środki ostrożności

1. Wyrób FemoSeal™ Vascular Closure System może być wszczepiany przez lekarzy, którzy zostali odpowiednio przeszkoleni w obsłudze urządzenia.

2. Przed wszczepieniem wyrobu FemoSeal™ Vascular Closure System należy wykonać angiogram tętnicy udowej lub nakłucie tętnicy udowej pod kontrolą ultrasonograficzną.
3. Przerwać procedurę, jeśli:
  - Światło tętnicy udowej wspólnej < 5 mm.
  - W okolicy miejsca nakłucia tętnicy udowej wspólnej występuje stenoza i/lub płytką o znacznej wielkości.
  - Nakłucie znajduje się na rozgałęzieniu tętnicy lub jest położone dystalnie względem tego rozgałęzienia.
  - W okolicy miejsca nakłucia tętnicy udowej wspólnej występują anomalne rozgałęzienia lub atypowe naczynia krwionośne.
4. Jeśli występuje krwiak, należy zachować szczególną ostrożność w celu prawidłowego wprowadzenia koszulki ze stożkową obudową do tętnicy.
5. Zastosować technikę nakłuwania jednościennej. Nie nakłuwać tylnej ścianki tętnicy.
6. Podczas użycia wyrobu FemoSeal™ Vascular Closure System zawsze przestrzegać techniki sterylnej.
7. Wyrób FemoSeal™ Vascular Closure System jest przeznaczony wyłącznie do jednorazowego użytku i nie należy go poddawać ponownej sterylizacji ani ponownie używać. System FemoSeal™ został zaprojektowany w taki sposób, że nie można go użyć ponownie.
8. Jeśli wszczepienie uszczelki wewnętrznej napotka nieoczekiwany opór, należy przerwać zabieg.
9. Aby prawidłowo założyć uszczelkę wewnętrzną, przesunąć kciuk w taki sposób, aby przycisk mógł swobodnie odskoczyć.
10. Przed wszczepieniem zewnętrznego krążka blokującego upewnić się, że koszulka ze stożkową obudową systemu FemoSeal™ znajduje się pod powierzchnią skóry. Zewnętrzny krążek blokujący może zostać przypadkowo umieszczony powyżej poziomu skóry u pacjentów z niewielką odległością między tętnicą udową a poziomem skóry.
11. W celu prawidłowego wszczepienia konieczne może być uprzednie nacięcie skóry.
12. Jeśli uszczelka wewnętrzna znajduje się wewnątrz tętnicy, ale nie jest możliwe całkowite wciśnięcie przycisku oraz wszczepienie zewnętrznego krążka blokującego, może być konieczne przeprowadzenie operacji w celu usunięcia elementów zamykających systemu FemoSeal™.

13. Jeśli w ciągu 18 miesięcy konieczne będzie nakłucie tej samej tętnicy udowej, należy je wykonać w odległości co najmniej jednego centymetra proksymalnie od poprzedniego miejsca dostępu wyrobu FemoSeal™ Vascular Closure System.
14. Poinstruować pacjenta, aby przestrzegał zaleceń lekarza dotyczących kontroli miejsca zamknięcia.
15. Poinstruować pacjenta, aby nosił kartę informacyjną dla pacjenta przez następne 18 miesięcy

### **Środki ostrożności w czasie wypisu**

Przed rozważeniem wypisu ocenić pacjenta pod kątem następujących warunków:

1. Krwawienie i/lub krwiak w miejscu zamknięcia.
2. Ból podczas chodzenia.
3. Oznaki infekcji w miejscu zamknięcia.

### **1.3.3 Działania korygujące dotyczące bezpieczeństwa**

W okresie od 1 września 2019 do 31 sierpnia 2024 doszło do jednego działania korygującego dotyczącego bezpieczeństwa stosowania systemu FemoSeal™ VCS.

W 2022 roku firma Terumo dobrowolnie wycofała system FemoSeal™ VCS z powodu skarg dotyczących nieudanych próbnych procesów i partii dla produktu FemoSeal firmy Elkton do pomiaru siły zgniatania i siły wycofywania. Z Korei Południowej wycofano łącznie 950 urządzeń.

## **1.4 Ocena kliniczna i badania kontrolne po wprowadzeniu wyrobu na rynek**

**Tabela 1.3** zawiera listę badań podstawowych, które umożliwiły wprowadzenie systemu FemoSeal™ VCS na rynek, a także badań przeprowadzonych po wprowadzeniu systemu na rynek oraz podjętych na ich podstawie działań klinicznych.

Wersja urządzenia używana w badaniu została uwzględniona w poniższej tabeli.

Pierwsza wersja systemu FemoSeal™ VCS (nr 11200) była dostępna na rynku do 2006 roku, a kolejna (nr C11202) została wprowadzona na rynek w 2006 roku i jest dostępna dotychczas.

**Tabela 1.3 Podsumowanie badań podstawowych**

| <b>Badania funkcjonalne na zwierzętach przed wprowadzeniem systemu na rynek</b>                                                                                                                                                                                         | <b>Wersja urządzenia</b> |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                    |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                    |



|                                                                                                                                                                                                                                                                 |                           |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                     |
| <b>Pierwsze badanie kliniczne na ludziach</b>                                                                                                                                                                                                                   |                           |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                    | 11200                     |
| <b>Ukończone badania kliniczne przeprowadzone po wprowadzeniu systemu na rynek</b>                                                                                                                                                                              |                           |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                                                                      | C11202<br>(obecna wersja) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                                                                               | C11202<br>(obecna wersja) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                                                                                                                                                  | C11202<br>(obecna wersja) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)                                                                                                                                          | C11202<br>(obecna wersja) |
| <b>Planowane / Trwające badania kliniczne przeprowadzone po wprowadzeniu systemu na rynek</b>                                                                                                                                                                   |                           |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                                                                                                                                                      | C11202<br>(obecna wersja) |
| <b>Działania kliniczne podjęte na podstawie badań, po wprowadzeniu systemu na rynek</b>                                                                                                                                                                         |                           |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                                                                                                                                                       | C11202<br>(obecna wersja) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                                                                                                                                                              | C11202<br>(obecna wersja) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024)                                                                                                                                 | C11202<br>(obecna wersja) |

#### 1.4.1 Podsumowanie danych z badań (na zwierzętach i badań klinicznych) przed wprowadzeniem wyrobu na rynek

W tabeli 1.4 poniżej opisano wszystkie badania przeprowadzone przed wprowadzeniem produktu na rynek, zarówno badania na zwierzętach, jak i kliniczne.

**Tabela 1.4 Podsumowanie badań przeprowadzonych przed wprowadzeniem na rynek**

| Badania funkcjonalne na zwierzętach przed wprowadzeniem systemu na rynek                                          |                                |                                               |                                                                                             |                                                                                                                              |                                                                                                                                                                            |
|-------------------------------------------------------------------------------------------------------------------|--------------------------------|-----------------------------------------------|---------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Nazwa badania                                                                                                     | Rok / CI                       | Nazwa badania                                 | Cele                                                                                        | Etapy                                                                                                                        | Potencjalne kryteria akceptacji                                                                                                                                            |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculture System. | 2000<br>Radi Medical System AB | Badanie na zwierzętach; badanie eksploracyjne | Celem badania była ocena biokompatybilności i biofunkcjonalności biodegradowalnego implantu | N = 3 dorosłe samice owcy, 1 zwierzę na punkt czasowy<br><br>Kontynuacja w zakresie analizy histopatologicznej, klasyfikacji | Drożność tętnicza<br>• Ocena przepływu krwi po wszczepieniu - zmniejszenie przepływu krwi o 2/3 w związku z tymczasowym skurczem naczyń tętniczych, spowodowanym zabiegiem |

|                                                                                                                                                      |                                   |  |                                                                                                                                                  |                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------|--|--------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | Wykonane przez Biomatech, Francja |  | zaprojektowanego w celu uzyskania hemostazy w układzie naczyniowym. Raport dotyczy zwierząt rezerwowych z badania numer 862 (dokument # 1051-01) | <p>makroskopowej i analizy ultrastrukturalnej</p> <ul style="list-style-type: none"> <li>• 12 miesięcy</li> <li>• 15 miesięcy</li> <li>• 18 miesięcy</li> </ul> <p>Ultradźwięki dopplerowskie — 30 dni w miejscach dostępu do tętnicy szyjnej i udowej</p> | <p>— oba wystąpiły w lewej tętnicy szyjnej wspólnej Dopplerowska ocena ultrasonograficzna (4 tygodnie) — 3/3 (100%) bez znacznej redukcji przepływu krwi 30 dni po wszczepieniu</p> <p>• Obserwacje makroskopowe</p> <ul style="list-style-type: none"> <li>• 12 miesięcy — drożność potwierdzona makroskopowo w wyniku braku widocznej okluzji anatomicznej; brak makroskopowych oznak lokalnej nietolerancji (krwotok, martwica lub neowaskularyzacja), zaobserwowano enkapsulację wewnętrznego krążka</li> <li>• 15 miesięcy — obserwacja makroskopowa nie wykazała oznak stanu zapalnego; nie zidentyfikowano żadnych pozostałości krążków wewnętrznych ani zewnętrznych; tkanka otaczająca znajdująca się w obszarze krążka zewnętrznego wyglądała tak samo, jak obserwacja 12-miesięczna</li> <li>• 18 miesięcy — obserwacja makroskopowa nie wykazała żadnych oznak lokalnej nietolerancji, widoczny zewnętrzny krążek (3/3 przypadki), całkowity rozkład krążka wewnętrznego zakończony; 1/3 (lewa tętnica szyjna wspólna) — zagłębienie ściany tętnicy zaobserwowane w miejscu wszczepienia implantu (może być związana z wszczepieniem urządzenia)</li> </ul> <p>Rezultaty</p> <ul style="list-style-type: none"> <li>• Makroskopowo, po 12, 15 i 18 miesiącach od wszczepienia nie wykryto objawów martwiczych, zwyrodnieniowych ani zakrzepowych.</li> <li>• Proces rozkładu krążków wewnętrznych i zewnętrznych przebiegał</li> </ul> |
|------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------|--|--------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                                                                                                                                                                                                                                                                                |                                                                             |                                                      |                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
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|                                                                                                                                                                                                                                                                                |                                                                             |                                                      |                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                        | <p>w okresie od 12 do 18 miesięcy i wydawał się zakończony po 18 miesiącach, przy czym biała tkanka pokrywała wszczepiony obszar.</p> <ul style="list-style-type: none"> <li>Pod względem histologicznym po 18 miesiącach materiał polimerowy nie był już widoczny, ale znajdowała się w nim endoluminalna włóknista tkanka. Nie zaobserwowano uszkodzeń martwiczych, zwyrodnieniowych ani zakrzepowych.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002 Radi Medical System AB</p> <p>Wykonane przez Biomatech, Francja</p> | <p>Badanie na zwierzętach; badanie eksploracyjne</p> | <p>Celem badania była ocena biokompatybilności biodegradowalnego implantu zaprojektowanego w celu uzyskania hemostazy w układzie naczyniowym.</p> | <p>Kontynuacja (po wszczepieniu)</p> <ul style="list-style-type: none"> <li>12 tygodni</li> <li>24 tygodni</li> <li>36 tygodni</li> </ul> <p>N = 12 owiec, 3 zwierzęta na punkt czasowy, 3 zwierzęta rezerwowe uśmiercone po 12, 15 i 18 miesiącach</p> <p>Miejsca implantacji — prawe i lewe tętnice udowe, prawe i lewe tętnice szyjne wspólne</p> <p>Kolorowa analiza dopplerem ultradźwiękowym</p> | <p><u>Drożność tętnic szyjnych i udowych po 4 tygodniach</u></p> <ul style="list-style-type: none"> <li>Znaczna redukcja przepływu u krwi 0/12 (0%)</li> </ul> <p><u>Brak znacznej redukcji przepływu krwi</u></p> <ul style="list-style-type: none"> <li>Poważne zaburzenia przepływu krwi związane z wprowadzeniem urządzenia 0/12 (0%)</li> <li>Redukcja przepływu krwi w lewej tętnicy szyjnej wspólnej 2/12 (16,6%) z powodu czasowego skurczu naczyń krwionośnych (spowodowanego zabiegiem chirurgicznym, a nie z urządzeniem)</li> </ul> <p><u>Oslabienie przepływu krwi</u></p> <p>12 tygodni — 0/12 (0%)<br/>24 tygodnie — 0/12 (0%)<br/>36 tygodnie — 0/12 (0%)</p> <p>Pomiar ciśnienia krwi (3 owce — 36 tygodni)</p> <ul style="list-style-type: none"> <li>Brak znacznej redukcji przepływu krwi</li> </ul> <p>Dane makroskopowe na potrzeby integracji i degradacji (stopień 0-4)</p> <p><u>Dostęp szyny</u></p> <p><u>Strona wewnętrzna</u> — enkapsulacja</p> <p>12 tygodni 1,3</p> |

|  |  |  |  |  | 24 tygodnie 0,8<br>36 tygodni 0,7<br>— rozkład materiału<br>12 tygodni 2,2<br>24 tygodnie 2,3<br>36 tygodni 0,7<br><i>Strona zewnętrzna</i><br>— enkapsulacja<br>12 tygodni 2,0<br>24 tygodnie 1,0<br>36 tygodni 0,8<br>— rozkład materiału<br>12 tygodni 2,0<br>24 tygodnie 2,7<br>36 tygodni 3,2<br><br><u>Dostęp udowy</u><br><i>Strona zewnętrzna</i><br>— enkapsulacja<br>12 tygodni 1,0<br>24 tygodnie 2,7<br>36 tygodni 1,0<br>— rozkład materiału<br>12 tygodni 2,0<br>24 tygodnie 2,4<br>36 tygodni 3,0<br><br><i>Strona wewnętrzna</i><br>— enkapsulacja<br>12 tygodni 2,0<br>24 tygodnie 1,2<br>36 tygodni 1,0<br>— rozkład materiału<br>12 tygodni 1,0<br>24 tygodnie 2,2<br>36 tygodni 3,0<br><br><u>Dane histologiczne dotyczące integracji, rozkładu i parametrów zapalnych (średnia istotnych wartości, indeks 0-4) n=6</u><br><br><u>Dostęp szyjny</u><br>Zwłóknienie zewnętrzne<br>12 tygodni — 2,3<br>24 tygodnie — 2,3<br>36 tygodni — 1,8<br>Neointima wewnętrzna<br>12 tygodni — 3,0<br>24 tygodnie — 2,7 |
|--|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | 36 tygodnie — 3,3<br>Rozkład materiału<br>12 tygodni — 1,7<br>24 tygodnie — 3,0<br>36 tygodni — 3 +<br>Parametry zapalne (makrofagi)<br>12 tygodni — 3,0<br>24 tygodnie — 1,7<br>36 tygodni — 1,7<br><u>Dostęp udowy</u><br>Zwłóknienie zewnętrzne<br>12 tygodni — 1,3<br>24 tygodnie — 1,5<br>36 tygodni — 1,7<br>Neointima wewnętrzna<br>12 tygodni — 3,7<br>24 tygodnie — 3,3<br>36 tygodni — 3,8<br>Rozkład materiału<br>12 tygodni — 2,0<br>24 tygodnie — 3,0<br>36 tygodni — 3+<br>Parametry zapalne (makrofagi)<br>12 tygodni — 3,5<br>24 tygodnie — 1,8<br>36 tygodni — 1,8<br><br><u>Wartości drożności histomorfologicznej</u><br>Dostęp szyjny<br>12 tygodni 74,0%<br>24 tygodnie 81,9%<br>36 tygodni -89,43%<br>Dostęp udowy<br>12 tygodni — 42,2%<br>24 tygodnie — 73,21%<br>36 tygodni — 78,71%<br><br><u>Drożność naczyń w USA (średnia %)</u><br>Dostęp szyjny<br>12 tygodni 94,6%<br>24 tygodnie — 96,7%<br>36 tygodni — 94,7%<br>Dostęp udowy<br>12 tygodni — 66,9%<br>24 tygodnie — 63,6%<br>36 tygodni — 75,1% |
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|                                                                                                                                                                                                                                                                        |                                                                                    |                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                 | <p>Rezultaty</p> <ul style="list-style-type: none"> <li>Nie wykryto znaczących objawów lokalnej nietolerancji (brak widocznych zmian zapalnych, martwiczych lub zwyrodnieniowych) po 12, 24 i 36 tygodniach</li> <li>Nie zarejestrowano istotnej niepożądanego reakcji tkankowej w odniesieniu do gospodarza i urządzenia</li> <li>Rozkład implantu był prawie zakończony po 36 tygodniach</li> </ul>                                                                                                                                                                                                                                                                                                                                                                       |
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| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002</p> <p>Radi Medical System AB</p> <p>Wykonane przez Biomatech, Francja</p> | <p>Badanie na zwierzętach</p> | <p>Celem badania była ocena biokompatybilności i biofunkcjonalności biodegradowalnego implantu zaprojektowanego w celu uzyskania hemostazy w układzie naczyniowym. Przebadany wyrób był przeznaczony do wprowadzenia w miejscu nakłucia tętnicy w celu uzyskania hemostazy. Jeden krążek wszedł do otworu w tętnicy, a drugi docisnął wewnętrzny krążek po zewnętrznej stronie tętnicy. Oba krążki zostały wprowadzone przez koszulkę introducera. Krążki zostały zaprojektowane w taki sposób, aby zapobiegać krwawieniu, zrosnąć się ze ścianą naczynia, a następnie ulec całkowitemu rozkładowi i wchłonięciu. Celem badania było zebranie i przeanalizowanie danych po funkcjonalnym wszczepieniu u owiec i świń w celu oceny zdolności implantu do utrzymania funkcji fizjologicznej podczas</p> | <p>Okres wszczepienia / obserwacji wynosi 5 tygodni dla wszystkich zwierząt</p> <p>4 owce, 1 świnia</p> <p>14 elementów zamykających</p> <p>8 elementów zamykających wszczepionych w 2 owcach</p> <p>2 elementy zamykające wszczepione w 1 świnie</p> <p>W przypadku wszczepienia dwóch elementów zamykających do tej samej tętnicy udowej, zostały one wszczepione w odległości &gt; 30 mm</p> | <p>Zarejestrowano wszelkie niepożądane oznaki (stan zapalny, martwica, krwotok lub inne zmiany chorobowe) oraz powstanie cienkiej wewnętrznej warstwy tętnicy. Szczególną uwagę zwrócono na początkową integrację tkanek, zwłaszcza na enkapsulację wewnętrznego krążka.</p> <p>Makroskopowo nie zaobserwowano znaczących objawów miejscowej nietolerancji ani tworzenia się skrzepin. Obserwacja makroskopowa nie ujawniła żadnej różnicy między owcą a świnie po wszczepieniu elementów zamykających w tętnicach udowych. Makroskopowo nie zaobserwowano znaczących objawów miejscowej nietolerancji ani tworzenia się skrzepin. Obserwacja makroskopowa nie ujawniła żadnej różnicy między owcą a świnie po wszczepieniu elementów zamykających w tętnicach udowych.</p> |

|  |  |  | stosowania w układzie krążenia, określenia reakcji gospodarza oraz reakcji wyrobu (integracja fizyczna, enkapsulacja tkanki po uśmierceniu) i oceny stopnia rozkładu implantu |  | <p>Badanie histopatologiczne miejsca wszczepienia implantu u owiec nie wykazało żadnych miejscowych reakcji niepożądanych. Wewnętrzne i zewnętrzne krążki wykazują oznaki rozkładu, a w niektórych przypadkach były rozbite na mniejsze części. Krążki wewnętrzne zostały całkowicie zintegrowane z tkanką neointymalną. W przypadku świni analiza histopatologiczna wykazała nieco więcej objawów zapalnych wokół krążka wewnętrznego i zewnętrznego. U obu zwierząt, w multifilamencie wykazano nieco więcej objawów zapalnych niż w materiale krążka, co jest normalne w przypadku plecionych nici chirurgicznych ze względu na ich większą powierzchnię.</p> <p>Drożność naczyń mierzono po 5 tygodniach przy użyciu trzech różnych metod: histomorfometrycznej i histomorfometrycznej w połączeniu z pomiarem średnicy naczyń za pomocą suwmiarki i kolorowej ultrasonografii dopplerowskiej. Średnia drożność naczyń u owiec wynosiła od 60 do 80% w zależności od metody (12 obserwacji). W przypadku świń średnia drożność naczyń wynosiła od 40 do 80% (2 obserwacje).</p> |
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| Pierwsze badanie kliniczne na ludziach                                                                                                                                                                       |                              |                                                 |                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
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| Nazwa badania                                                                                                                                                                                                | Rok / CI                     | Nazwa badania                                   | Cele                                                                                                                                                                                                                                                                                                       | Etapy                                                                                                                                                                                                                                                                                                                                                                                               | Potencjalne kryteria akceptacji                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Badanie otwarte, jednoramienn e, wieloośrodkowe | Celem badania było określenie bezpieczeństwa, wydajności i działania wyrobu FemoSeal Vascular Closure System (system FemoSeal) w ujęciu ogólnym, a w szczególności elementów zamykających u pacjentów poddawanych kardiologicznym zabiegom diagnostycznym lub interwencyjnym z dostępem do tętnicy udowej. | <p>Badanie 2-częściowe</p> <p>Łącznie n = 80</p> <p>Część 1 n = 20</p> <p>Część 2 n = 60</p> <p>Wskazania:</p> <p>Część 1 — diagnostyczne cewnikowanie serca z wykorzystaniem tętnicy udowej jako miejsca dostępu</p> <p>Część 2 — pacjenci poddawani diagnostycznym i interwencyjnym zabiegom kardiologicznym z zastosowaniem tętnicy udowej jako miejsca dostępu</p> <p>Kontrola po 30 dniach</p> | <p>Rezultaty</p> <p><u>Hemostaza uzyskana z FS bez ucisku</u></p> <p>— Część 1 20/20 (100%)</p> <p>— Część 2 58/60 (97%)</p> <p>Mediana czasu do hemostazy w czasie zabiegu (część 2) — 1,0 minuty (zakres natychmiastowy — 8 minut)</p> <p><u>Czas do mobilizacji (minuty)</u></p> <p>Część 1 —</p> <p>Mediana: 33,0</p> <p>Średnia: 67,8</p> <p>Część 2 —</p> <p>mediana: 45</p> <p>Średnia: 87,5</p> <p><u>Częstość poważnych powikłań naczyniowych — 30-dniowa obserwacja</u></p> <p>Część 1</p> <p>— Bez powikłań naczyniowych 20/20 (100%)</p> <p>Część 2</p> <p>Tętniak rzekomy — 1/59 (1,69%)</p> <p><u>Niepowodzenie leczenia</u></p> <p>Część 1 — 0/20 (0%)</p> <p>Część 2 — 3/60 (5%)</p> <ul style="list-style-type: none"> <li>2 z powodu nieosiągnięcia hemostazy bez zastosowania ucisku</li> <li>1 z powodu poważnych powikłań naczyniowych, tętniaka rzekomego</li> </ul> |



|  |  |  |  |  | <p><u>Ciągły wysięk</u></p> <p>Część 1 — 0/20 (0%)</p> <p>Część 2 — 8/60 (13%)</p> <p><u>Krwiak</u></p> <p>Część 1 — 0/20 (0%)</p> <p>Część 2 — 6/60 (10%)</p> |
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W ramach wstępnego planu rozwoju systemu FemoSeal™ VCS przeprowadzono 3 testy funkcjonalne na zwierzętach. W 2000 roku przed rozpoczęciem badań klinicznych przeprowadzono badanie na zwierzętach w celu oceny biofunkcjonalności systemu FemoSeal™ VCS. W tym badaniu oceniono zdolność elementów zamykających do utrzymania funkcji fizjologicznej oraz poziom ich rozkładu. Po 18 miesiącach materiał krążka wewnętrznego i zewnętrznego nie był już widoczny i został zastąpiony endoluminalną włóknistą tkanką. Podsumowując, potwierdzono zdolność elementu zamykającego systemu FemoSeal™ VCS do utrzymania funkcji fizjologicznej podczas stosowania w układzie krążenia.

W 2002 roku przeprowadzono badanie na zwierzętach w celu oceny biokompatybilności i biofunkcjonalności biodegradowalnego implantu, systemu FemoSeal™ VCS, zaprojektowanego w celu uzyskania hemostazy w układzie naczyniowym. W skrócie: degradacja implantu była prawie zakończona przed upływem 36 tygodni i nie wystąpiła żadna znacząca niepożądana reakcja tkankowa.

W kolejnym badaniu na zwierzętach przeprowadzonym w 2002 roku dokonano oceny biokompatybilności i biofunkcjonalności biodegradowalnego implantu, systemu FemoSeal™ VCS, zaprojektowanego w celu uzyskania hemostazy w układzie naczyniowym. Po 5 tygodniach enkapsulacja krążka była zakończona i zaobserwowano oznaki rozkładu zarówno krążka wewnętrznego, jak i zewnętrznego. Podsumowując, potwierdzono zdolność implantu do utrzymania funkcji fizjologicznej po zastosowaniu w układzie krążenia.

W ramach planu rozwoju klinicznego systemu FemoSeal™ VCS firma Radi Medical System AB przeprowadziła wstępne badanie kliniczne. To badanie kliniczne nie zostało opublikowane ani udostępnione w Internecie. Badanie z użyciem modelu urządzenia #11200 zostało przeprowadzone w 2002-2004 r. zgodnie z normą europejską EN 540 (Badanie kliniczne wyrobów medycznych dla ludzi) oraz zgodnie z ogólnymi uwagami ICH dotyczącymi badań klinicznych i zasadami dobrej praktyki klinicznej. Szczegóły tego badania zostały udokumentowane w raporcie EU-SE-001. Badanie kliniczne zostało udokumentowane w końcowym sprawozdaniu firmy Radi Medical Systems AB, „Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After

Diagnostic/Interventional Cardiology Procedures”. Badanie kliniczne przeprowadzono na pierwszym modelu urządzenia FemoSeal™ #11200, koncentrując się na bezpieczeństwie i skuteczności wszczepialnych elementów zamykających. Jediną różnicą między pierwszym modelem #11200 a obecnym modelem C11202 jest rozmiar French, odpowiednio 6F i 7F, oraz ulepszony system podawania. Korzyści kliniczne, przeznaczenie, sposób działania oraz surowce, z których wykonane są wszczepialne elementy zamykające, wewnętrzne uszczelka i zewnętrzny krążek blokujący pozostają niezmienione.

Urządzenie przeznaczone było do stosowania u pacjentów poddawanych diagnostycznym zabiegom kardiologicznym lub interwencyjnym z wykorzystaniem tętnicy udowej jako punktu dostępu. Celem tego badania było określenie bezpieczeństwa, działania i efektywności systemu FemoSeal™ VCS. Było to prospektywne, wieloośrodkowe, jednoramienne badanie otwarte z 30-dniową obserwacją.

Głównym punktem końcowym badania w zakresie działania był czas do hemostazy zdefiniowanej jako brak aktywnego krwawienia. Głównym punktem końcowym badania w zakresie bezpieczeństwa były przypadki poważnych powikłań naczyniowych w okresie 30 dni. Poboczne punkty końcowe obejmowały czas do mobilizacji, odsetek nieskutecznych terapii, częstotliwość występowania zdarzeń niepożądanych oraz charakterystykę działania urządzenia podczas wprowadzania i wszczepiania.

Pacjentami biorącymi udział w tym badaniu byli dorośli, którzy byli w stanie udzielić świadomej zgody, z tętnem na tętnicy grzbietowej przynajmniej jednej stopy. Pacjenci zostali wykluczeni z badania, jeśli cierpieli na którąkolwiek z poniższych chorób:

- Historia chorób naczyń obwodowych
- Choroby autoimmunologiczne
- Znane zaburzenie krwawienia spowodowane ciężką anemią
- INR >1,5
- Zawał mięśnia sercowego w ciągu poprzednich 72 godzin
- Niekontrolowane nadciśnienie pomimo leczenia
- Otyłość wykluczająca dostęp techniką Seldingera
- Obecność przeszczepu naczyniowego lub stentu w miejscu arteriotomii
- Wcześniejsze nakłucie ipsilateralne w ciągu poprzednich 3 miesięcy
- Przewidywany okres życia < 6 miesięcy

Dodatkowo pacjenci zostali zbadani śródoperacyjnie i wykluczeni z badania w przypadku zaobserwowania któregoś z poniższych objawów:

- Światło tętnicy udowej wspólnej < 5 mm
- Rozgałęzienia tętnicy w odległości 2 cm proksymalnie do miejsca wkłucia

- Znaczące zwężenie w odległości 3 cm od miejsca wkłucia
- Użycie koszulki głównego introduktora >6 Fr
- Nakłucie na rozgałęzieniu tętnicy lub położone dystalnie względem tego rozgałęzienia.
- Wielokrotne nakłucie tętnicy udowej
- Znane lub podejrzewane nakłucie ściany tylnej tętnicy udowej
- Duży krwiak (2:6 cm) po zakończeniu zabiegu
- Trudność z wprowadzeniem koszulki do zabiegu z powodu krętej tkanki lub naczynia

Badanie było oparte na pojedynczym protokole i zostało przeprowadzone w dwóch częściach:

W 1. części zakwalifikowano 20 pacjentów, następnie przeprowadzono analizę bezpieczeństwa, a w 2. części zakwalifikowano kolejnych 60 pacjentów.

W 1. części średni wiek pacjentów wynosił 65,9 roku, 70,0% pacjentów stanowili mężczyźni, a 95% jednocześnie pacjentów przyjmowało leki. W 2. części badania średni wiek pacjentów wynosił 63,8 roku, 78% pacjentów stanowili mężczyźni, a 100% jednocześnie przyjmowało leki.

Pacjenci poddani zabiegowi cewnikowania serca w celach diagnostycznych (część 1 i część 2) i interwencyjnych (część 2) byli uprawnieni do udziału w badaniu. Sposób postępowania był zgodny ze standardem opieki w każdym ze szpitali uczestniczących w badaniu, a następnie zastosowano system FemoSeal™ VCS. Dane pacjenta zostały zebrane na początku procedury, w jej trakcie oraz 1 dnia i 30 dni po zabiegu. Wyniki podsumowano w **tabeli 1.5** i wskazano, że FemoSeal™ VCS jest bezpieczny i skuteczny w użyciu w tej grupie pacjentów.

**Tabela 1.5 Wyniki kliniczne badania przeprowadzonego przed wprowadzeniem na rynek**

|                                                                                                                                       | Część 1     | Część 2                  |
|---------------------------------------------------------------------------------------------------------------------------------------|-------------|--------------------------|
| Liczba pacjentów                                                                                                                      | 20          | 60                       |
| Średni czas do hemostazy                                                                                                              | 1,2 minuty  | 1,6 minuty <sup>a</sup>  |
| Średni czas do mobilizacji                                                                                                            | 72,2 minuty | 87,5 minuty <sup>b</sup> |
| Częstość występowania poważnych powikłań naczyniowych <sup>c</sup>                                                                    | 0 (0%)      | 1 (2%)                   |
| Liczba pacjentów z zdarzeniem niepożądanym                                                                                            | 5 (25%)     | 19 (32%)                 |
| Nieprowadzenie leczenia (definiowane jako poważne powikłania naczyniowe, potrzeba ucisku manualnego lub oba te problemy jednocześnie) | 0 (0%)      | 3 (5%)                   |
| Usterki urządzenia                                                                                                                    | 0 (0%)      | 6 (10%)                  |

*<sup>a</sup>Na podstawie próby 58 pacjentów, ponieważ u 2 pacjentów nie uzyskano hemostazy w czasie zabiegu z powodu wcześniejszych nakłuć ipsilateralnych. U tych pacjentów uzyskano hemostazę po 7 minutach i 37 minutach.*

*<sup>b</sup>Na podstawie próby 59 pacjentów: 1 pacjent nie został uwzględniony, ponieważ podłączono go pod respirator z powodu obrzęku płuc i nie mógł się poruszać przez ponad tydzień.*

*<sup>c</sup>Zdefiniowano jako powikłania naczyniowe wymagające transfuzji krwi lub zabiegu chirurgicznego albo miejscowe zakażenie wymagające podania antybiotyku, hospitalizacji lub przedłużenia hospitalizacji, albo opracowanie rany*

W 1. części badania nie zaobserwowano poważnych powikłań naczyniowych. W 2. części badania odnotowano 1 poważne powikłanie naczyniowe: tętniak rzekomy zgłoszony w ciągu 1 dnia po zabiegu. Zdarzenie wymagało ucisku pod kontrolą ultradźwięków oraz wstrzyknięcia trombiny do tętniaka rzekomego, co przedłużyło hospitalizację pacjenta.

Spośród 5 zdarzeń niepożądanych zgłoszonych w 1. części badania 1 było potencjalnie związane z zastosowaniem urządzenia: aktywne krwawienie w ciągu 1 dnia po zabiegu (niesklasyfikowane jako poważne). Spośród 19 działań niepożądanych zgłoszonych w 2. części badania zaobserwowano 3 zdarzenia niepożądane związane z urządzeniem (niesklasyfikowane jako poważne) w postaci krwaka, a także 6 zdarzeń potencjalnie związanych z urządzeniem (niesklasyfikowanych jako poważne): 3 zgłoszenia uporczywego wysięku, 2 krwaki i 1 ból nogi po ćwiczeniach.

W 2. części badania leczenie 3 pacjentów uznano za nieudane: w 2 przypadkach w związku z nieosiągnięciem hemostazy bez zastosowania ucisku, a w 1 w związku z poważnym powikłaniem naczyniowym (tętniak rzekomy). W 1. części badania nie stwierdzono przypadków nieudanego leczenia.

Spośród sześciu przypadków wadliwego działania urządzenia w 2. części badania trzy nie zakłóciły zabiegu, jeden został spowodowany błędem użytkownika, jeden poległ na nieszczelności introducera, a jeden na pękniętym mocowaniu filamentu. Ostatnie dwa problemy zostały rozwiązane poprzez aktualizację modelu wprowadzoną w C11202.

2. części badania klinicznego przeprowadzonego przed wprowadzeniem urządzenia na rynek nie uwzględniono 6-miesięcznych wyników badań kontrolnych z powodu nieprzestrzegania zaleceń przez pacjentów. 30-dniowe wyniki badania klinicznego przeprowadzonego przed wprowadzeniem urządzenia na rynek (EU-SE-001), zgodne z okresem obserwacji stosowanym w literaturze klinicznej, wykazały, że system FemoSeal™ VCS jest bezpieczny i skuteczny.

#### **1.4.2 Podsumowanie danych z badań klinicznych po wprowadzeniu produktu na rynek**

W tabeli 1.6 poniżej opisano 4 zakończone badania kliniczne przeprowadzone po wprowadzeniu systemu na rynek. Te badania kliniczne nie zostały opublikowane ani udostępnione w Internecie.

**Tabela 1.6 Ukończone badania kliniczne przeprowadzone po wprowadzeniu systemu na rynek**

| Ukończone badania kliniczne przeprowadzone po wprowadzeniu systemu na rynek                    |                                                             |                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|------------------------------------------------------------------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|----|-----|----------|-------|----------|-----------|----|-----------|-----------|-------------------------|----------|--------------------|------------|---------------------|-----------|-------------------|---------|-----------------------|----------|--------------------------------|----------|----------------------|-----------|--------------------------|-----------|-----------------------------------|----------|----------------------|--------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Nazwa badania                                                                                  | Rok / CI                                                    | Nazwa badania                                                                                               | Cele                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Etapy                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Potencjalne kryteria akceptacji                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)<br>User Acceptability of New Packaging (SIS) (2006) | 2006<br><br>RADI                                            | Badanie przeprowadzone po wprowadzeniu systemu na rynek, akceptowalność nowego opakowania przez użytkownika | Badanie po wprowadzeniu systemu na rynek przeprowadzono na podstawie aktualizacji modelu FemoSeal Vascular® #11202, który ma zmodyfikowany system podawania w porównaniu z pierwszym modelem, nr 11200, aby udokumentować jego funkcjonalność.<br><br>Celem badania było uzyskanie informacji zwrotnej na temat poprawionej instrukcji obsługi (IO), projektu szkoleniowego dla lekarzy i pielęgniarek, potwierdzenie ocen dokonanych w analizie ryzyka oraz przekazanie informacji na temat poprawy jakości produktu. | 100 pacjentów <ul style="list-style-type: none"><li>63 mężczyzn / 37 kobiet</li><li>Średni wiek kobiet 68 lat, mężczyzn 65 lat</li></ul> 2 szwedzkie szpitale, 6 lekarzy<br><br>112 urządzeń<br><br>Dane zarejestrowane na formularzach danych pacjenta (CRF)<br><br>Planowany czas obserwacji — 30 minut od momentu zastosowania                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Rezultaty<br><br>1. Ilustracje/Polecenia zawarte w instrukcji obsługi zostały uznane za informacyjne i odpowiednie<br><br>2. Natychmiastowa hemostaza (91/100) |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)              | Dr Nicolas Moes, Uniwersytet Medyczny w Innsbrucku, Austria | Potwierdzenie oceny wyrobu po wprowadzeniu na rynek                                                         | Celem tego badania była ocena bezpieczeństwa i działania systemu FemoSeal® stosowanego w normalnej praktyce klinicznej u pacjentów poddawanych kardiologicznym zabiegom diagnostycznym lub interwencjom przezskórnym z wykorzystaniem koszulki 7F.                                                                                                                                                                                                                                                                     | 50 kolejnych pacjentów<br><br>Wskazanie — diagnostyczne lub inwazyjne cewnikowanie serca z tętnicy udowej wspólnej<br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.6±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±8.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>56 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                                              | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.6±11.1 | body mass index (kg/m²) | 25.4±8.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 56 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Główne punkty końcowe <ul style="list-style-type: none"><li>Główny punkt końcowy w zakresie skuteczności — TTH (czas do hemostazy) z wysiękiem lub bez, ale bez dodatkowego ucisku manualnego ani mechanicznego.</li><li>Punkt końcowy w zakresie bezpieczeństwa — częstotliwość występowania zdarzeń niepożądanych — drobne i poważne powikłania naczyniowe oraz wszystkie inne zdarzenia niepożądane — poważne i niepożądane w trakcie trwania badania (tj. do momentu wypisania pacjenta).</li></ul> Rezultaty <ul style="list-style-type: none"><li>Średni czas do hemostazy</li></ul> |
| n                                                                                              | 50                                                          |                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| men                                                                                            | 35 (70%)                                                    |                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| women                                                                                          | 15 (30%)                                                    |                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| PCI cases                                                                                      | 15                                                          |                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| age (yrs)                                                                                      | 62.6±11.1                                                   |                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| body mass index (kg/m²)                                                                        | 25.4±8.7                                                    |                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| systolic BP (mmHg)                                                                             | 131.2±20.9                                                  |                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| diastolic BP (mmHg)                                                                            | 77.9±10.6                                                   |                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| diabetes mellitus                                                                              | 9 (18%)                                                     |                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| arterial hypertension                                                                          | 34 (68%)                                                    |                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| previous coronary intervention                                                                 | 13 (26%)                                                    |                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| preprocedure aspirin                                                                           | 50 (100%)                                                   |                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| preprocedure clopidogrel                                                                       | 56 (100%)                                                   |                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Procedural unfractionated heparin                                                              | 15 (30%)                                                    |                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Procedural abciximab                                                                           | 2 (4%)                                                      |                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |

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|                                                                                |           |                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                               | <ul style="list-style-type: none"> <li>• Diagnostyka — <math>56,6 \pm 29</math> sekund</li> <li>• Interwencja — <math>59,9 \pm 16,2</math> sekundy</li> <li>• Wszyscy pacjenci <math>57,8 \pm 26,3</math></li> <li>• Wszyscy pacjenci zostali zmobilizowani po 4 godzinach wypoczynku w łóżku bez żadnych problemów.</li> </ul> <p>Wyniki bezpieczeństwa</p> <ul style="list-style-type: none"> <li>• 49/50 (98%) bez powikłań naczyniowych do wypisu ze szpitala</li> <li>• Średni czas do wypisu 2,6 dnia</li> <li>• 1/50 (2%) niewielkie krwawienie następnego dnia po bezproblemowej mobilizacji w dniu angiografii</li> </ul>                                                 |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009) | 2009 RADI | Badanie po wprowadzeniu na rynek | <p>Badanie ma na celu sprawdzenie, czy klienci/użytkownicy doświadczyli problemów z nowym opakowaniem, zwłaszcza z niesterylną zewnętrzną stroną woreczka Tuvek/PET-PE.</p> <p>Badanie powinno również dostarczyć informacji na temat tego, czy lekarz prowadzący dostrzega jakieś różnice w zastosowaniu/wszczeniu urządzenia w porównaniu z poprzednio stosowanymi urządzeniami.</p> <p>Badanie powinno również dostarczyć informacji na temat dalszych potrzeb związanych z poprawą jakości produktów.</p> | <p>25 urządzeń</p> <p>4 szwedzkie szpitale</p> <p>16/25 (64%) pacjentów stanowili pacjenci PCI przyjmujący ciężkie leki przeciwzakrzepowe</p> | <p>Rezultaty</p> <ol style="list-style-type: none"> <li>1. Problemy związane z opakowaniem — 21/25 (84%) przypadków użycia zakończyło się powodzeniem; 4/25 (16%) przypadki nie powiodły się (1 — testowanie nowego introducera, 1 wewnętrzny krążek przeszedł przez arteriotomię na etapie wycofania, przycisk wyskoczył, a zewnętrzny krążek został umieszczony w kanale tkanki nacięcia, 2 natychmiastowa hemosta za nie została osiągnięta pomimo bezproblemowego wszczepienia).</li> <li>2. Natychmiastowa hemosta za 19/25 (76%) pacjentów</li> <li>3. Krwawienie 11/25 (44%) — 9/25 (36%) wysięk/krwawienie, krwaki 2/25 (8%)</li> </ol> <p>Łączny wskaźnik zdarzeń 19%</p> |

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| <p>The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022)</p> | <p>2022/<br/>Terumo<br/>Medical Corporation</p> | <p>Prospektywne, wieloośrodkowe badanie obserwacyjne po wprowadzeniu produktu na rynek</p> | <p>Dalsze zademonstrowanie bezpieczeństwa i skuteczności systemu FemoSeal™ VCS w osiąganiu hemostazy miejsc dostępu w tętnicy udowej wspólnej (CFA) u rzeczywistych pacjentów poddawanych przezskórnym zabiegom wewnątrznaczyniowym.</p> | <ul style="list-style-type: none"> <li>Wizyta kontrolna po 30 dniach (<math>\pm 7</math> dni) w szpitalu lub przez telefon.</li> <li>Rejestracja: od grudnia 2021 r. do lipca 2022 r.</li> <li>Planowany u 230 zarejestrowanych pacjentów poddawanych diagnostycznym lub interwencyjnym zabiegom wewnątrznaczyniowym z wykorzystaniem urządzenia FemoSeal™.</li> </ul> <p>3 zakłady europejskie: Francja (92 pacjentów), Niemcy (38 pacjentów), Belgia (100 pacjentów).</p> | <ul style="list-style-type: none"> <li><b>Dane demograficzne / choroby współistniejące:</b> <ul style="list-style-type: none"> <li>Płeć: 161 mężczyzn (70%) / 69 kobiet (30%).</li> <li>Średni wiek: <math>70 \pm 12</math>.</li> <li>BMI: <math>26,1 \pm 4,95</math> kg/m<sup>2</sup>.</li> <li>Nadciśnienie: 160 pacjentów (69,6%).</li> <li>Dyslipidemia: 128 (55,7%).</li> <li>Choroba tętnicy wieńcowej: 42 (18,3%).</li> <li>Obecny palacz: 86 (37,6%).</li> <li>Były palacz: 66 (28,8%).</li> <li>Choroba wieńcowa serca: 34 (14%).</li> <li>Zawał mięśnia sercowego w wywiadzie: 18 (7,8%).</li> <li>Rewaskularyzacja tętnicy obwodowej: 12 (5,2%)</li> <li>tętnicy szyjnej i 83 (37,5%) tętnicy kończyny dolnej.</li> <li>Terapia przeciwplatekowa (początkowa): 211 (91,7%), w tym 21 (9,1%) podwójna terapia przeciwplatekowa (DAPT).</li> <li>Antykoagulacja, doustnie: 40 pacjentów (17,4%).</li> </ul> </li> <li><b>Charakterystyka ingerencji:</b> <ul style="list-style-type: none"> <li>Okoliczności: 162 przypadki w szpitalu (70,4%), 68 przypadków w ambulatorium (29,6%).</li> <li>Przeważające wskazanie: chromanie 147 przypadków (63,9%).</li> <li>Sposób postępowania: 35 przypadków dostępu przedniego (15,3%), 194 przypadki dostępu wstecznego (84,7%).</li> </ul> </li> <li><b>Główne punkty końcowe:</b> <ul style="list-style-type: none"> <li>Łączny punkt końcowy bezpieczeństwa (brak</li> </ul> </li> </ul> |
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|  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
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|  |  |  |  |  | <p>poważnych powikłań w miejscu dostępu w ciągu 6 godzin po zabiegu) i skuteczności (skuteczna hemostaza w miejscu wkłucia) osiągnięto u 215/226 (95,1%) [95% CI: 91,46; 97,55]</p> <p>pacjentów w pełnym zestawie danych oraz u 215/230 (93,5%) [95% CI 89,47, 96,30]</p> <p>pacjentów w zestawie leczonym FemoSeal™.</p> <p>- Punkt końcowy skuteczności został osiągnięty u 219/226 (96,9%) CI [93,7, 98,7] pacjentów.</p> <p>- Punkt końcowy bezpieczeństwa osiągnięty u 220/230 (95,2%) [95% CI: 92,15, 97,90] pacjentów.</p> <p>• <b>Drugie punkty końcowe:</b></p> <p>- Brak drobnych powikłań w miejscu dostępu przez sześć godzin po zabiegu uzyskano u 225/230 (97,8%) [95% CI: 95,00; 99,29] pacjentów.</p> <p>- Brak poważnych i drobnych powikłań w miejscu dostępu od sześciu godzin do 30 dni po zabiegu uzyskano u 219/230 (95,2%) [95% CI: 91,60; 97,59] pacjentów.</p> <p>- Mediana czasu do hemostazy z systemem FemoSeal™ VCD: 0,42 (0,25; 0,50) minuty.</p> <p>- Mediana czasu do mobilizacji: 5,00 (4,54; 5,50) minuty.</p> <p>- Mediana czasu hospitalizacji: 23,98 (22,72, 25,00) godzin.</p> <p>- Łatwość użycia systemu FemoSeal™ VCS:</p> |
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|  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                         |
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|  |  |  |  |  | <p>„łatwe” lub „bardzo łatwe” wdrożenie w 98,7% przypadków („łatwe” wdrożenie w 21 (9,2%) przypadkach, „bardzo łatwe” wdrożenie w 205 (89,5%) przypadkach przy braku lub niskim oporze podczas wdrożenia w 226 (98,3%) przypadkach.</p> <p>152/230 (66,1%) pacjentów leczonych przy użyciu przewodnika z zestawem FemoSeal™ (GW 0,038") i zalecanego w zestawie FemoSeal™ bez zgłaszanych wad urządzenia lub zdarzeń niepożądanych.</p> |
|--|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Badanie z 2006 r. zostało przeprowadzone w celu potwierdzenia bezpieczeństwa i skuteczności obecnego urządzenia z ulepszonym systemem dostarczania oraz uzyskania informacji zwrotnej na temat instrukcji obsługi i programu szkoleniowego FemoSeal™ VCS. Badanie obejmowało 100 pacjentów, a głównym punktem końcowym było to, czy osiągnięto hemostazę, czy też potrzebny był dodatkowy ucisk manualny lub mechaniczny. Badanie wykazało, że zastosowanie systemu FemoSeal™ VCS zakończyło się powodzeniem w większości przypadków (91% osiągnęło natychmiastową hemostazę).

W badaniu przeprowadzonym w 2008 r. na próbie 50 pacjentów oceniono bezpieczeństwo i działanie systemu FemoSeal™ VCS w normalnej praktyce klinicznej u pacjentów poddanych cewnikowaniu serca za pomocą koszulki o rozmiarze 7 Fr. Głównym punktem końcowym w badaniu były zgromadzone dane dotyczące czasu do hemostazy oraz czasu do mobilizacji bez dodatkowego ucisku manualnego ani mechanicznego. Wyniki badania wykazały, że średni czas do hemostazy wynosił 57,8 sekundy, a wszyscy pacjenci odzyskali sprawność ruchową po 4 godzinach odpoczynku w łóżku.

Celem badania z 2009 roku była ocena nowego opakowania FemoSeal™ VCS. Do badania zakwalifikowano 25 pacjentów. Głównym punktem końcowym w badaniu było to, czy użytkownik doświadczył jakichkolwiek problemów z opakowaniem. Użytkownicy nie zauważyli żadnych problemów z nowym opakowaniem FemoSeal™ VCS. W tym badaniu zebrano również dane dotyczące upływu czasu do osiągnięcia hemostazy.

Celem badania z 2022 roku było proaktywne zgromadzenie danych dotyczących bezpieczeństwa i skuteczności systemu FemoSeal VCS w osiąganiu hemostazy miejsc dostępu

w tętnicy udowej wspólnej (CFA) u rzeczywistych pacjentów poddawanych przezskórnym zabiegom wewnątrznaczyniowym. Do badania zakwalifikowano 230 pacjentów. Głównymi punktami końcowym dla tego badania są: powodzenie zabiegu (tj. osiągnięcie hemostazy w miejscu wkłucia) oraz ograniczenie poważnych powikłań (np. uszkodzenie naczyń krwionośnych, krwawienie w miejscu wkłucia, powtórny ucisk manualny, nowe ostre niedokrwienie kończyny dolnej związane z miejscem dostępu). Badanie wykazało, że system FemoSeal™ VCS działa dobrze w rzeczywistych warunkach i zapewnia skuteczną hemostazę oraz niskie wskaźniki powikłań w miejscu dostępu u pacjentów poddawanych zabiegom wewnątrznaczyniowym w naczyniach obwodowych. System FemoSeal™ VCS wykazuje dobre działanie z krótkim czasem do hemostazy i dobrymi informacjami zwrotnymi od operatorów, co sprawia, że jest cennym urządzeniem do zamykania dostępu udowego.

### 1.4.3 Podsumowanie danych z kontroli klinicznych po wprowadzeniu produktu na rynek

#### 1.4.3.1 Zakończone działania kliniczne podjęte na podstawie badań, po wprowadzeniu systemu na rynek

Podsumowanie przeprowadzonych klinicznych działań kontrolnych po wprowadzeniu produktu na rynek zostało opisane w **tabeli 1.7** poniżej.

**Tabela 1.7. Działania kliniczne podjęte na podstawie badań, po wprowadzeniu systemu na rynek**

| Zakończone działania kliniczne podjęte na podstawie badań, po wprowadzeniu systemu na rynek |             |                                                                         |                                                                                                                                                                                                                |                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                          |
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| Nazwa działania                                                                             | Rok/CI      | Nazwa badania                                                           | Cele                                                                                                                                                                                                           | Etapy                                                                                                                                                         | Potencjalne kryteria akceptacji                                                                                                                                                                                                                                                                                                                                                                                                          |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021)                   | 2021<br>TMC | Badanie kliniczne po wprowadzeniu u na rynek – badanie wysokiej jakości | Badanie po wprowadzeniu na rynek w celu zebrania potencjalnych informacji zwrotnych dotyczących stosowania urządzenia do zamykania naczyń krwionośnych FemoSeal™ dystrybuowanego na rynkach Unii Europejskiej. | <ul style="list-style-type: none"> <li>120 przypadków</li> <li>8 wyjątkowych lekarzy z &gt; 5 latami doświadczenia</li> <li>Wiele krajów w Europie</li> </ul> | <p><b>Ocena urządzenia w skali 1-5 — Odpowiedzi otwarte</b></p> <ul style="list-style-type: none"> <li>Kryteria dopuszczalności <ul style="list-style-type: none"> <li>Oceny 3-5 są uznawane za korzystne</li> <li>Wszystkie odpowiedzi otwarte powinny zawierać ≥ 80% pozytywnych opinii</li> </ul> </li> <li>Rezultaty <ul style="list-style-type: none"> <li>Nie otrzymano żadnej odpowiedzi zawierającej &gt;</li> </ul> </li> </ul> |

| Zakończone działania kliniczne podjęte na podstawie badań, po wprowadzeniu systemu na rynek                                     |                  |                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
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|                                                                                                                                 |                  |                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                            | 20% niekorzystnych opinii <ul style="list-style-type: none"> <li>Brak skarg dotyczących produktu</li> </ul>                                                                                                                                                                                                                                                                                                                                                             |
| 20210298 – 0.035” and 0038” Guidewire Clinical Survey Report (2021)                                                             | 2021 TMC         | Badanie kliniczne po wprowadzeniu na rynek – badanie wysokiej jakości | Badanie po wprowadzeniu na rynek mające na celu zebranie potencjalnych informacji zwrotnych dotyczących stosowania prowadnika 0,035” dołączonego do urządzenia 6Fr Angio-Seal™ VIP Vascular Closure Device (VCD) oraz prowadnika 0,038” dołączonego zarówno do urządzenia 8Fr Angio-Seal™ VIP VCD, jak i systemu FemoSeal Vascular Closure System dystrybuowanego na rynkach Unii Europejskiej. | <ul style="list-style-type: none"> <li>Ankiety dotyczące prowadnika 0,035” <ul style="list-style-type: none"> <li>106 ankiet</li> <li>64 lekarzy</li> </ul> </li> <li>Ankiety dotyczące prowadnika 0,038” <ul style="list-style-type: none"> <li>109 ankiet</li> <li>55 lekarzy</li> </ul> </li> <li>12 ankiet retrospektywnych</li> </ul> | <b>Ocena urządzenia w skali 1-5 — Odpowiedzi otwarte</b> <ul style="list-style-type: none"> <li>Kryteria dopuszczalności <ul style="list-style-type: none"> <li>Oceny 3-5 są uznawane za korzystne</li> <li>Wszystkie odpowiedzi otwarte powinny zawierać ≥ 80% pozytywnych opinii</li> </ul> </li> <li>Rezultaty <ul style="list-style-type: none"> <li>Wszystkie prowadniki otrzymały pozytywne oceny</li> <li>Brak skarg dotyczących produktu</li> </ul> </li> </ul> |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023–2024 TMC/TE | Badanie kliniczne po wprowadzeniu na rynek – badanie wysokiej jakości | Prospektywne zbieranie informacji zwrotnych dotyczących stosowania systemu FemoSeal VCS z prowadnikami dystrybuowanymi na rynku UE.                                                                                                                                                                                                                                                             | <ul style="list-style-type: none"> <li>126 ankiet</li> <li>Placówki</li> <li>5 krajów</li> <li>14 listopada 2023 - 11 czerwca 2024</li> <li>Specjalizacja medyczna: <ul style="list-style-type: none"> <li>Chirurgia naczyniowa</li> <li>Radiologia interwencyjna</li> <li>Angiologia</li> </ul> </li> </ul>                               | <b>Ocena urządzenia w skali 5-stopniowej — Odpowiedzi otwarte</b> <ul style="list-style-type: none"> <li>Kryteria dopuszczalności <ul style="list-style-type: none"> <li>Oceny 3-5 są uznawane za korzystne</li> <li>Wszystkie odpowiedzi otwarte powinny zawierać ≥ 80% pozytywnych opinii</li> </ul> </li> <li>Jeśli w ramach tej ankiety wystąpią zdarzenia niepożądane, powinny</li> </ul>                                                                          |

| Zakończone działania kliniczne podjęte na podstawie badań, po wprowadzeniu systemu na rynek |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
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|                                                                                             |  |  |  |  | <p>to być zdarzenia przewidywane w ramach zarządzania ryzykiem.</p> <ul style="list-style-type: none"> <li>Dane demograficzne pacjentów: <ul style="list-style-type: none"> <li>Kobieta: 29,4% (37/126)</li> <li>Mężczyzna: 69,8% (88/126)</li> <li>Płeć nieujawniona: 0,8 (1/126)</li> <li>Wiek &gt;75 lat: 31,7%</li> </ul> </li> <li>Rezultaty <ul style="list-style-type: none"> <li>Prowadnik dostarczony z systemem FemoSeal™ VCS: 101/126 (80,2%).</li> <li>Maksymalny czas trwania procedury (minuty): 63,4 (36,6) (średnia (SD)); 57,0 (36,–81,0) (mediana (IQR))</li> <li>Wszystkie oceny skuteczności systemu FemoSeal™ VCS były pozytywne.</li> <li>Wszystkie oceny prowadnika dostarczonego z systemem FemoSeal™ VCS były korzystne.</li> </ul> </li> </ul> |

| Zakończone działania kliniczne podjęte na podstawie badań, po wprowadzeniu systemu na rynek |  |  |  |  |                                                                                                                                                                                                                                                                                                                                 |
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|                                                                                             |  |  |  |  | <ul style="list-style-type: none"> <li>○ Jedno zdarzenie niepożądane (0,8%): krążki systemu FemoSeal™ VCS nie były prawidłowo ustawione prawdopodobnie z powodu użycia sztywnego o przewodnika (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 cala) wymagającego ręcznego ucisku w celu osiągnięcia hemostazy.</li> </ul> |

Firma Terumo Medical Corporation przeprowadziła trzy wysokiej jakości ankiety dla użytkowników medycznych w bieżącym okresie sprawozdawczym (od 1 września 2019 r. do 31 sierpnia 2024 r.).

Badania kliniczne FemoSeal™ zgromadziły proaktywne dane kliniczne dotyczące bezpieczeństwa i działania systemu FemoSeal™ VCS w zastosowaniach klinicznych. Badanie zawierało pytania dotyczące całego urządzenia i powiązanych z nim akcesoriów, w tym przewodnika 0,038" oraz ich bezpośrednich interakcji. Badania kliniczne dotyczące przewodnika zebrały dane kliniczne dotyczące bezpieczeństwa i działania przewodnika 0,038" dostarczonego z systemem FemoSeal™ VCS w zastosowaniach klinicznych. Pytania zawarte w ankiecie dotyczyły konkretnie ogólnego zastosowania przewodnika, począwszy od wprowadzenia przez koszulkę zabiegową do układu naczyniowego, a skończywszy na jego wysunięciu.

System FemoSeal™ VCS z dołączonym przewodnikiem 0,038" otrzymały same pozytywne oceny, a także wpłynęło 6 (sześć) reklamacji dotyczących urządzenia oraz 9 (dziewięć) zgłoszeń niereklamacyjnych dotyczących przewodnika nad podstawie ewaluacji uwag otrzymanych z wysokiej jakości ankiet klinicznych. Reklamacje zostały ocenione zarówno dla systemu

FemoSeal, jak i dla przewodnika, i rozpatrzono je w ramach procesu nadzoru po wprowadzeniu produktu na rynek. Nie zidentyfikowano nowych zagrożeń ani poziomów ryzyka.

Ankieta dla użytkowników medycznych została przeprowadzona w 2024 roku w ramach działań PMCF. Wyniki badania wykazały, że ogólna ocena skuteczności i bezpieczeństwa systemu FemoSeal™ VCS była bardzo pozytywna. Wykazano również kompatybilność przewodników innych niż standardowe przewodniki dostarczane z systemem FemoSeal™ VCS.

#### **1.4.3.2 Bieżąca/Planowana kontrola kliniczna po wprowadzeniu na rynek**

TMC ma jedno bieżące/planowane działania kontrolne po wprowadzeniu wyrobu na rynek. Zostanie przeprowadzona ankieta kliniczna mająca na celu prospektywne gromadzenie informacji zwrotnych dotyczących zastosowania przewodnika dostarczanego z systemem FemoSeal VCS na rynku UE. Ankieta jest przeznaczona dla lekarzy i ma na celu sprawdzenie, jakich przewodników używają podczas zabiegu. Celem tej ankiety jest wyeliminowanie luki zidentyfikowanej jako brak literatury i komentarzy recenzentów zewnętrznych dotyczących zgodności systemu FemoSeal™ VCS z użyciem przewodników innych marek niż Terumo. Informacje zwrotne obejmują wyniki techniczne, działanie kliniczne i bezpieczeństwo związane z działaniem urządzenia z wykorzystaniem różnych przewodników.

#### **1.4.4 Podsumowanie danych z systematycznego przeglądu literatury**

Terumo Medical Corporation systematycznie przegląda literaturę w celu gromadzenia i oceny danych dotyczących bezpieczeństwa i skuteczności z opublikowanych badań dotyczących produktu FemoSeal™ VCS i/lub podobnych urządzeń. Celem rocznego przeglądu literatury fachowej jest zidentyfikowanie wcześniej nieznanymi działań niepożądanych, monitorowanie znanych skutków ubocznych, rozpoznawanie pojawiających się zagrożeń oraz identyfikacja możliwości systematycznego niewłaściwego użycia lub zastosowania produktu FemoSeal™ VCS.

Ostatni systematyczny przegląd literatury, który obejmował okres od 1 września 2019 do 31 sierpnia 2024 pozwolił odnaleźć 29 opublikowanych badań, które dostarczyły danych na temat bezpieczeństwa i skuteczności produktu FemoSeal™ VCS. W dziewięciu badaniach zgłoszono dwadzieścia trzy przypadki prawidłowego i nieprawidłowego stosowania systemu FemoSeal™ VCS. Ogólnie rzecz biorąc, przegląd publikacji odnoszących się do badań dotyczących zastosowania systemu FemoSeal™ VCS ukazuje reprezentatywną populację pacjentów z UE poddanych zabiegowi przezskórnego cewnikowania naczyniowego. Lista 23 recenzowanych publikacji dotyczących użytku zgodnie z przeznaczeniem znajduje się w **części 3**.

Działanie kliniczne oceniono za pomocą następujących środków:

- Czas do hemostazy jest lepszy lub porównywalny ze znanymi przypadkami przezskórnego zamknięcia tętnicy udowej wspólnej.

- Czas do odzyskania sprawności ruchowej jest lepszy lub porównywalny ze znanymi przypadkami przezskórnego zamknięcia tętnicy udowej wspólnej.
- Częstość powikłań pooperacyjnych jest porównywalna lub niższa od obecnych standardów opieki.

Na podstawie tych parametrów działania klinicznego oraz danych pozyskanych z literatury klinicznej stwierdzono, że system FemoSeal™ VCS może być z powodzeniem używany do zamknięcia nakłucia tętnicy udowej (arteriotomii) u pacjentów, którzy przeszli cewnikowanie przezskórne przy użyciu koszulki zabiegowej o rozmiarze 7 Fr lub mniejszym. Całkowita hemostaza została osiągnięta u większości pacjentów (79,65–100%) i była powiązana z medianą czasu do hemostazy wynoszącą 0,5 min, czyli średnim czasem do wypisu wynoszącym 3 dni. Pomiędzy 69,2 a 86,7% pacjentów było w stanie poruszać się 5 godzin po zamknięciu rany, przy średnim pooperacyjnym spoczynku w łóżku wynoszącym 349 minut. Niepowodzenie systemu FemoSeal™ VCS zaobserwowano w 3,68–4% przypadków, a dodatkowy ucisk ręczny był wymagany dla 0,9–4,4% zabiegów.

Bezpieczeństwo kliniczne oceniono na podstawie zdarzeń niepożądanych, w tym między innymi:

- Krwawienie
- Krwiak
- Tętniak rzekomy
- Zasinienie
- Przetoka tętniczo-żylna
- Infekcja
- Zgon

Dla każdego z tych zdarzeń niepożądanych częstość występowania raportowana dla systemu FemoSeal™ VCS była mniejsza lub porównywalna z wcześniej raportowanym wskaźnikiem dla ucisku manualnego i innych urządzeń do zamykania naczyń.

Nie zidentyfikowano żadnych działań niepożądanych w analizie 10 przypadków, ponieważ nie zidentyfikowano żadnego nowego, nieprzewidzianego ani niedopuszczalnego ryzyka.

Ogólna skuteczność stosowania systemu FemoSeal™ VCS podczas angiografii diagnostycznej lub zabiegów interwencyjnych zależy od wielu czynników, takich jak płeć, wiek, anatomia pacjenta, choroby współistniejące, anatomiczne umiejscowienie miejsca wkłucia, doświadczenie chirurga, metoda rozmieszczenia VCD, opieka pooperacyjna, itp. Oprócz sukcesu technicznego, w tym osiągnięcia hemostazy, system FemoSeal™ VCS zapewniał korzyści kliniczne w odniesieniu do zamknięcia naczynia po nakłuciu tętnicy udowej, takie jak skrócenie czasu do hemostazy, skrócenie czasu do mobilizacji. Wyniki osiągnięte dla systemu FemoSeal™ VCS są



zgodne z wynikami oczekiwanymi dla tego wyrobu, używanego zgodnie z przeznaczeniem. Niektóre z referencji uzyskanych w bieżącym okresie wyszukiwania wykazały zastosowanie badanego urządzenia w lokalizacji anatomicznej innej niż tętnica udowa wspólna oraz do zamykania arteriotomii > 7 Fr, co jest uważane za niezgodne z przeznaczeniem.

Podczas przeglądu nie stwierdzono żadnych nieznanych skutków ubocznych, pojawiających się zagrożeń ani możliwego systematycznego niewłaściwego użycia urządzenia. Jeśli jednak system FemoSeal™ VCS jest używany z ostrożnością przez przeszkolonych lekarzy, wyrób medyczny działa jako użyteczny i niezbędny wyrób kliniczny. Ogólnie rzecz biorąc, terapia docelowa, a tym samym system FemoSeal™ VCS, odpowiada na obecną potrzebę kliniczną w leczeniu powikłań związanych z dostępem naczyniowym.

Ogólnie rzecz biorąc, dane zawarte w literaturze nie pozwoliły zidentyfikować żadnych, nieznanych wcześniej, problemów z działaniem ani bezpieczeństwem w warunkach klinicznych ani niekorzystnych efektów, które występowałyby z częstotliwością przekraczającą oczekiwania / dopuszczalne normy. W związku z tym na podstawie literatury można stwierdzić, że system FemoSeal™ VCS, używany do uzyskiwania hemostazy poprzez ucisk arteriotomii po cewnikowaniu przezskórnym, działa zgodnie z oczekiwaniami i nie powoduje poważnych zdarzeń niepożądanych związanych z bezpieczeństwem.

#### 1.4.5 Podsumowanie danych z badań nadzoru po wprowadzeniu produktu na rynek

Wdrożono proaktywny system PMS, a wszystkie reklamacje są weryfikowane co miesiąc, zgodnie z wewnętrznymi procedurami produkcyjnymi. Dane z reklamacji zostały przeanalizowane w okresie od 1 września 2019 r. do 31 sierpnia 2024 r. Ogólnie rzecz biorąc, do producenta dotarło 28 raportów dotyczących nadzoru nad wyrobami medycznymi (MDV) oraz 476 reklamacji konsumenckich. Spośród 28 zgłoszeń MDV, 27 było związanych ze zdarzeniami niepożądanymi, a jedno z nieprawidłowym działaniem wyrobu. W okresie sprawozdawczym wystąpiły dwa zgony, ale żaden ze zgłoszonych zgonów nie został uznany za związany z badanym wyrobem. Spośród 476 reklamacji złożonych do wytwórcy najczęstszą przyczyną reklamacji były trudności z wdrożeniem (146 przypadków, wskaźnik występowania 0,0142%). Tryb awarii zdarzeń wyciągania jest drugim najczęściej występującym z odsetkiem 0,0126% (130 zdarzeń).

Na całym świecie sprzedano ponad 1 030 136 sztuk wyrobu FemoSeal™ Vascular Closure System, z czego 827 843 w Europejskim Obszarze Gospodarczym. Obliczona częstotliwość reklamacji w oparciu o sprzedaż globalną wynosi 0,046%. Całkowity wskaźnik reklamacji konsumenckich jest bardzo niski. Nie zidentyfikowano nowych zagrożeń, które nie zostały uwzględnione w instrukcji obsługi i dokumentacji ryzyka.

Częstotliwość występowania działań niepożądanych przedstawiono w **tabeli 1.2**. W ramach reklamacji nie zidentyfikowano nowych nieprzewidzianych, przyszłych ani niedopuszczalnych zagrożeń. Nie zaobserwowano znaczącego wzrostu częstotliwości ani nasilenia znanych niepożądanych działań niepożądanych.



#### 1.4.6 Ogólne podsumowanie działania klinicznego i bezpieczeństwa

System FemoSeal™ VCS służy do zamykania nakłucia (arteriotomii) tętnicy udowej wspólnej u pacjentów, u których wykonano cewnikowanie przezskórne przy użyciu koszulki zabiegowej o średnicy 7F (2,33 mm) lub mniejszej. Ta ocena kliniczna opiera się na kompleksowej analizie danych klinicznych dostępnych przed wprowadzeniem wyrobu na rynek i po jego wprowadzeniu oraz na literaturze dotyczącej zamierzonego zastosowania wyrobu FemoSeal™ VCS.

Przeprowadzono kompleksowy przegląd opublikowanej literatury obejmujący okres od 1 września 2019 r. do 31 sierpnia 2024 r. Zbiór dowodów objął 29 badań dotyczących systemu FemoSeal™ VCS. Dowody przedstawione w ocenie klinicznej wskazują, że poddawany badaniu wyrób jest bezpieczny i skuteczny, gdy jest stosowany zgodnie z przeznaczeniem, a wszelkie zagrożenia lub niepożądane skutki uboczne, które mogą być związane z wyrobem w normalnych warunkach użytkowania, stanowią akceptowalne ryzyko w porównaniu z korzyściami, które przynoszą pacjentom. Wyniki osiągnięte dla badanych wyrobów są zgodne z wynikami oczekiwanymi dla tego typu wyrobów, używanych zgodnie z przeznaczeniem.

Potencjalne niepożądane skutki uboczne związane ze stosowaniem systemu FemoSeal™ VCS obejmują zdarzenia niepożądane najczęściej zgłaszane odnośnie do alternatywnych sposobów zamknięcia arteriotomii, np. krwawienie i krwiak. Ogólnie rzecz biorąc, częstotliwość występowania działań niepożądanych zgłaszanych w związku z użyciem systemu FemoSeal™ VCS jest podobna jak w przypadku ucisku manualnego i podobnych urządzeń do zamykania naczyń. Odnośnie do krwawienia i krwiaków liczba zgłoszeń dotyczących systemu FemoSeal™ VCS jest mniejsza niż w przypadku urządzeń do zamykania naczyń. Każde z działań niepożądanych, zgłoszonych w dostępnych publikacjach lub w ramach nadzoru po wprowadzeniu wyrobu na rynek, było znane już wcześniej (patrz **część 1.3**).

Dostępne dane dotyczące bezpieczeństwa klinicznego i działania FemoSeal VCS sugerują, że korzyści dla pacjenta wynikające z zastosowania tego urządzenia do zamykania naczyń krwionośnych przewyższają możliwe zagrożenia, gdy jest ono używane zgodnie z instrukcją użycia.

Jak wskazano w poprzednich rozdziałach, zgromadzone dane dotyczące systemu FemoSeal™ VCS potwierdzają spójność danych dotyczących ocenianego wyrobu (np. użycia wyrobu, wyników bezpieczeństwa, skuteczności klinicznej i korzyści klinicznych), zidentyfikowanych wyrobów równoważnych oraz danych dotyczących podobnych wyrobów wymienionych w podsumowaniu bieżącej wiedzy technicznej.

Analiza krzyżowa danych dotyczących bezpieczeństwa nie wykazała żadnych luk pomiędzy:

- danymi wymienionymi w podsumowaniu bieżącej wiedzy technicznej
- danymi specyficznymi dla ocenianego urządzenia
- danymi wymienionymi w plikach zarządzania ryzykiem

- danymi wymienionymi na etykiecie i/lub w instrukcji obsługi (tj. zagrożenia resztkowe, które należy przekazać użytkownikowi).

Bezpieczeństwo kliniczne zostało wykazane na podstawie niskiego wskaźnika powikłań zidentyfikowanych w opublikowanej recenzowanej literaturze klinicznej, sponsorowanych badaniach klinicznych oraz przeglądzie danych zgromadzonych po wprowadzeniu produktu na rynek — w zestawieniu z brakiem konieczności wycofania produktu z rynku. Nie stwierdzono żadnych obaw dotyczących skuteczności systemu FemoSeal™ VCS, a przegląd literatury obejmował tylko takie zastosowania, które były zgodne z przeznaczeniem określonym przez wytwórcę.

### 1.5 Możliwe alternatywy diagnostyczne lub terapeutyczne

Ucisk ręczny jest tradycyjnie stosowany w celu uzyskania hemostazy w miejscu arteriotomii po cewnikowaniu naczynia. Ucisk ręczny jest związany z unieruchomieniem pacjenta na dłuższy czas (do 8 godzin po zabiegu), a także znacznym dyskomfortem i dłuższym okresem hospitalizacji. Przeprowadzony niedawno przegląd systematyczny wykazał, że mediana czasu do osiągnięcia hemostazy metodą ucisku ręcznego wynosiła 20,8 minuty.<sup>1</sup>

Alternatywnym rozwiązaniem dla ucisku ręcznego są zewnętrzne urządzenia hemostatyczne, które stosują ucisk mechaniczny w miejscu arteriotomii. Urządzenia te nie skracają czasu do hemostazy ani czasu do mobilizacji pacjenta, ale zmniejszają obciążenie personelu poprzez zastąpienie ucisku manualnego uciskiem mechanicznym. Częstotliwość występowania zdarzeń niepożądanych związanych z zastosowaniem ucisku mechanicznego jest podobna jak w przypadku ucisku ręcznego.

Urządzenia do zamykania naczyń krwionośnych, takie jak system FemoSeal™ VCS, są przeznaczone do zamykania arteriotomii. Ich celem jest skrócenie czasu do hemostazy i umożliwienie wcześniejszej mobilizacji pacjenta. Przeprowadzony niedawno przegląd systematyczny, w którym sprawdzono 13 dostępnych na rynku urządzeń, wykazał, że mediana czasu do osiągnięcia hemostazy metodą ucisku ręcznego wynosiła 5,4 minuty. Mediana czasu do hemostazy dla poszczególnych urządzeń do zamykania naczyń wahała się od 1 minuty (FemoSeal™ VCS) do 14 minut; przy czym dla większości urządzeń wynosiła od 4 do 10 minut.<sup>1</sup>

Do często zgłaszanych zdarzeń niepożądanych związanych z zamknięciem arteriotomii metodą ucisku manualnego, przy użyciu zewnętrznych urządzeń hemostatycznych lub urządzeń do zamykania naczyń należą: krwiak, krwawienie w miejscu dostępu, tętniak rzekomy, przetoka tętniczo-żylna i infekcja. W tym samym przeglądzie systematycznym (34 randomizowane badania kontrolowane, 14 401 pacjentów) stwierdzono, że częstotliwość występowania zdarzeń niepożądanych była podobna pomiędzy uciskiem manualnym a urządzeniami do zamykania naczyń, z tym wyjątkiem, że krwawienie było nieco większe w przypadku urządzeń do zamykania naczyń.<sup>1</sup>

*1. Cox, T., L. Blair, C. Huntington, A. Lincourt, R. Sing, i B.T. Heniford. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Sugerowany profil i szkolenie użytkownika

Przewidywanymi użytkownikami wyrobu FemoSeal™ Vascular Closure System są lekarze przeszkoleni w zakresie uzyskiwania dostępu tętniczego i zamykania naczyń po zabiegach wewnątrznaczyniowych wykonywanych przez tętnicę udową wspólną, którzy ukończyli szkolenie lekarzy w zakresie obsługi systemu FemoSeal™ organizowane przez Terumo Medical Corporation.

## 1.7 Odpowiednie normy zharmonizowane i wspólne

| Oznaczenie normy | Bieżący rok zgodności/wersja | Opis                                                                                                                                     |
|------------------|------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070        | 2014/AMD1:2018               | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070     | 2014/A1:2018                 | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance     | 20 maja 2021                 | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052       | 2015                         | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213       | 2017                         | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503       | 2020                         | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182       | 2019                         | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |

| Oznaczenie normy | Bieżący rok zgodności/wersja | Opis                                                                                                                                                                     |
|------------------|------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 13485     | 2016/A11:2021                | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 13485        | 2016                         | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 14644-1      | 2015                         | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1   | 2015                         | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2      | 2015                         | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2   | 2015                         | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3      | 2019                         | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3   | 2019                         | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1      | 2003                         | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1   | 2003                         | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2      | 2003/TC1:2004                | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |

| Oznaczenie normy     | Bieżący rok zgodności/wersja | Opis                                                                                                                                          |
|----------------------|------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 14698-2       | 2003/TC 1:2004               | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| USP <788>            | ND.                          | PARTICULATE MATTER IN INJECTIONS                                                                                                              |
| Farmakopea UE 2.9.19 | ND.                          | Particulate Contamination: Sub-Visible Particles                                                                                              |
| IEC 62366-1          | 2015                         | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN 62366-1           | 2015                         | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN ISO 14971         | 2019/A11:2021                | Medical devices — Application of risk management to Medical devices                                                                           |
| ISO 14971            | 2019                         | Medical devices — Application of risk management to Medical devices                                                                           |
| ASTM F1980           | 2016                         | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                                           |
| EN ISO 10993-1       | 2020                         | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                    |
| ISO 10993-1          | 2018                         | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                    |
| EN ISO 10993-2       | 2006                         | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                                                |
| ISO 10993-2          | 2006                         | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                                                |
| EN ISO 10993-3       | 2014                         | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity                          |
| ISO 10993-3          | 2014                         | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity                          |

| Oznaczenie normy | Bieżący rok zgodności/wersja | Opis                                                                                                           |
|------------------|------------------------------|----------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-4   | 2017                         | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood               |
| ISO 10993-4      | 2017                         | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood               |
| EN ISO 10993-5   | 2009                         | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                             |
| ISO 10993-5      | 2009                         | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                             |
| EN ISO 10993-6   | 2016                         | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                  |
| ISO 10993-6      | 2016                         | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                  |
| EN ISO 10993-10  | 2023                         | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                 |
| ISO 10993-10     | 2021                         | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                 |
| EN ISO 10993-11  | 2018                         | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                |
| ISO 10993-11     | 2017                         | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                |
| EN ISO 10993-12  | 2021                         | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                 |
| ISO 10993-12     | 2021                         | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                 |
| EN ISO 10993-17  | 2009                         | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances |
| ISO 10993-17     | 2002                         | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances |

| Oznaczenie normy | Bieżący rok zgodności/wersja | Opis                                                                                                                                                                         |
|------------------|------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-18     | 2020/A1:2022                 | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-18  | 2020/A1:2022                 | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-23  | 2021                         | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23     | 2021                         | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382       | 2018                         | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756        | 2017                         | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>         | ND.                          | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>        | ND.                          | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72   | 2019                         | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135     | 2014/A1:2019                 | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135        | 2014/A1:2018                 | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |

| Oznaczenie normy | Bieżący rok zgodności/wersja | Opis                                                                                                                                                            |
|------------------|------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-7   | 2008/A1:2022                 | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                       |
| ISO 10993-7      | 2008/A1:2019                 | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                               |
| EN 556-1         | 2024                         | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices |
| EN ISO 11737-1   | 2018/A1:2021                 | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11737-1      | 2018/A1:2021                 | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| EN ISO 11138-1   | 2017                         | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-1      | 2017                         | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| EN ISO 11138-2   | 2017                         | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 11138-2      | 2017                         | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| EN ISO 15223-1   | 2016                         | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| ISO 15223-1      | 2016                         | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| EN 1041          | 2008/A1:2013                 | Information supplied by the manufacturer of medical devices                                                                                                     |



| Oznaczenie normy  | Bieżący rok zgodności/wersja | Opis                                                                                                                                                                       |
|-------------------|------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 11607-1    | 2020/A1:2023                 | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| ISO 11607-1       | 2019/A1:2023                 | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| EN ISO 11607-2    | 2020/A1:2023                 | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ISO 11607-2       | 2019/A1:2023                 | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169        | 2016                         | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M | 2016                         | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825        | 2018                         | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096        | 2011 (R 2019)                | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M     | 2015                         | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24      | 2021                         | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3       | 2020                         | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |
| MDCG 2020-8       | 2020                         | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                             |

| Oznaczenie normy | Bieżący rok zgodności/wersja | Opis                                                                                                                                                                                                                                                          |
|------------------|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-7      | 2020                         | Post-market clinical follow-up (PMCF) Plan Template<br>A guide for manufacturers and notified bodies                                                                                                                                                          |
| MDCG 2020-6      | 2020                         | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                                                                                                          |
| MDCG 2019-9 v1   | 2022                         | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                                                                                      |
| MDCG 2019-8 v2   | 2020                         | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15     | 2020                         | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11     | 2021                         | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19     | 2021                         | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4   | 2021                         | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2      | 2019                         | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1      | 2019                         | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7      | 2018                         | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6      | 2018                         | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device                                                                                                                                                                |

| Oznaczenie normy    | Bieżący rok zgodności/wersja | Opis                                                                                                                                                                                          |
|---------------------|------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                     |                              | Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                                                  |
| MDCG 2018-4         | 2018                         | MDCG 2018-4 Annex: UDI database<br>Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                               |
| MDCG 2018-3 v1      | 2020                         | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25        | 2021                         | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2.12-2 Rev 2 | 2012                         | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                        |

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### 3.0 HISTORIA ZMIAN

| Numer wersji SSCP       | Data wydania     | Opis zmiany                                                            | Wersja zatwierdzona przez jednostkę notyfikowaną                                                                                                                                                                                                                                                                                                              |
|-------------------------|------------------|------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022            | 20 stycznia 2023 | Pierwsze wydanie, po certyfikacji MDR CE                               | <p><input checked="" type="checkbox"/> Tak</p> <p>Język weryfikacji: English</p> <p><input type="checkbox"/> Nie (dotyczy tylko urządzeń wszczepialnych klasy IIa lub niektórych IIb (MDR, artykuł 52 (4) 2. ustęp), dla których SSCP nie zostało jeszcze zatwierdzone przez jednostkę notyfikowaną)</p> <p><input type="checkbox"/> Inne (proszę podać):</p> |
| SSCP-FS-2023 – Wersja 1 | 15 marca 2024    | Zaktualizowano dla okresu od 1 stycznia 2019 r. do 31 grudnia 2023 r.  | <p><input checked="" type="checkbox"/> Tak</p> <p>Język weryfikacji: English</p> <p><input type="checkbox"/> Nie (dotyczy tylko urządzeń wszczepialnych klasy IIa lub niektórych IIb (MDR, art. 52 pkt 4. akapit 2), dla których SSCP nie zostało jeszcze zatwierdzone przez jednostkę notyfikowaną)</p> <p><input type="checkbox"/> Inne (proszę podać):</p> |
| SSCP-FS-2024 Wersja 1   |                  | Zaktualizowano dla okresu od 1 września 2019 r. do 31 sierpnia 2024 r. | <p><input type="checkbox"/> Tak</p> <p>Język weryfikacji: English</p> <p><input type="checkbox"/> Nie (dotyczy tylko urządzeń wszczepialnych klasy IIa lub niektórych IIb (MDR, art. 52 pkt 4. akapit 2), dla których SSCP nie zostało jeszcze zatwierdzone przez jednostkę notyfikowaną)</p> <p><input type="checkbox"/> Inne (proszę podać):</p>            |

|                          |               |                                                            |                                                                                                                                                                                                                                                                                                                                                                      |
|--------------------------|---------------|------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>wersja 2 | June 20, 2025 | Zmieniono na podstawie<br>zapytań NSAI w celu<br>walidacji | <input checked="" type="checkbox"/> Tak<br>Język weryfikacji: English<br><br><input type="checkbox"/> Nie (dotyczy tylko urządzeń<br>wszczepialnych klasy IIa lub<br>niektórych IIb (MDR, art. 52<br>pkt 4. akapit 2), dla których<br>SSCP nie zostało jeszcze<br>zatwierdzone przez jednostkę<br>notyfikowaną)<br><br><input type="checkbox"/> Inne (proszę podać): |
|--------------------------|---------------|------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|



## Resumo do Desempenho Clínico e de Segurança

### FemoSeal™ Vascular Closure System

|                                                                              |                                                                                             |
|------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|
| <b>Fabricante</b>                                                            | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 EUA         |
| <b>NUR do fabricante</b>                                                     | US-MF-000019594                                                                             |
| <b>Representante da Administração/PRRC</b>                                   | Kimberly Feitl<br>Vice President, Quality                                                   |
| <b>Basic UDI-DI</b>                                                          | 38970FS79                                                                                   |
| <b>Número EMDN</b>                                                           | C900199 – Sistemas de hemóstase – Outros                                                    |
| <b>Classe do dispositivo</b>                                                 | Classe III                                                                                  |
| <b>Ano em que o dispositivo foi marcado pela primeira vez com a marca CE</b> | 2005                                                                                        |
| <b>Representante UE</b>                                                      | Terumo Europe N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Bélgica<br>NUR: BE-AR-000001433 |
| <b>Organismo notificado</b>                                                  | NSAI<br>CE 0050                                                                             |

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Este Resumo do desempenho clínico e de segurança (SSCP) destina-se a fornecer acesso público a um resumo atualizado dos principais aspetos do desempenho clínico e de segurança do FemoSeal™ Vascular Closure System (VCS).

Na **Secção 1.0** é fornecido um resumo do desempenho clínico e de segurança do dispositivo, destinado a utilizadores/profissionais de saúde.

## **1.0 RESUMO PARA UTILIZADORES/PROFISSIONAIS DE SAÚDE**

O SSCP não se destina a substituir as Instruções de utilização como documento principal para garantir a utilização segura do dispositivo, nem se destina a fornecer sugestões terapêuticas ou de diagnóstico a utilizadores previstos ou pacientes. O SSCP não se destina a substituir a informação obrigatória nos cartões de implante ou em qualquer outro documento obrigatório.

### **1.1 Utilização prevista do dispositivo**

#### **1.1.1 Utilização prevista**

O FemoSeal™ Vascular Closure System é um dispositivo médico destinado à oclusão de uma punção arterial após cateterização percutânea através da artéria femoral comum.

#### **1.1.2 Indicações de utilização**

O FemoSeal™ Vascular Closure System está indicado para utilização na oclusão da punção arterial femoral comum (arteriotomia) em pacientes que tenham sido submetidos a cateterização percutânea utilizando uma bainha de procedimento de 7F (2,33 mm) ou mais pequena.

#### **1.1.3 Contraindicações e/ou limitações**

O FemoSeal™ Vascular Closure System é contraindicado para pacientes com arteriotomias nas quais tenham sido utilizados bainhas ou dispositivos superiores a 7F (2,33 mm).

#### **1.1.4 Populações de pacientes alvo**

A segurança e eficácia do FemoSeal™ Vascular Closure System foi estabelecida em pacientes com 18 anos de idade ou mais, que foram submetidos a cateterização percutânea utilizando uma bainha de procedimento de 7F (2,33 mm) ou mais pequena.

#### **1.1.5 Populações especiais de pacientes**

A segurança e eficácia do FemoSeal™ Vascular Closure System não foram estabelecidas nas seguintes populações de pacientes:

- Pacientes com doenças autoimunes pré-existentes.
- Pacientes sujeitos a trombólise terapêutica.
- Pacientes com doença vascular periférica clinicamente significativa.
- Pacientes com hipertensão não controlada (sistólica > 220 mmHg ou diastólica > 110 mmHg).
- Pacientes com distúrbios hemorrágicos, incluindo trombocitopenia (contagem de plaquetas < 100.000) ou anemia (Hgb < 10 mg/dl).

- Pacientes com um lúmen interior da artéria femoral comum inferior a 5 mm.
- Pacientes com insuficiência renal e/ou hepática.
- Pacientes com outras comorbidades relevantes.
- População com origens raciais e/ou étnicas específicas.
- Pacientes com enfarte do miocárdio no prazo de 72 horas.
- Pacientes com um enxerto vascular ou stent no local da punção.
- Pacientes grávidas ou lactantes.
- Pacientes com idade inferior a 18 anos.

### 1.1.6 Utilizadores previstos

Os utilizadores previstos do FemoSeal™ Vascular Closure System são médicos com formação que os qualifica para a realização do acesso arterial e oclusão de procedimentos endovasculares através da artéria femoral comum e que tenham participado num programa de instruções para médicos sobre o FemoSeal™ da Terumo Medical Corporation.

## 1.2 Descrição do dispositivo

### 1.2.1 Descrição do dispositivo

O FemoSeal™ Vascular Closure System, fabricado pela Terumo Medical Corporation (TMC), é um dispositivo de oclusão vascular reabsorvível concebido para alcançar a hemóstase arterial femoral após cateterização percutânea através da artéria femoral comum.

Os elementos de oclusão FemoSeal™ são compostos por dois discos de polímero reabsorvíveis, pelo vedante interno e pelo disco de bloqueio externo, que são mantidos unidos por um multifilamento reabsorvível, selando assim mecanicamente a arteriotomia (ver **Figura 1.1** e **Figura 1.2**). Depois de ter sido colocado através da bainha do invólucro do cone, o disco de bloqueio externo é comprimido na haste do multifilamento, resultando na oclusão mecânica do ponto de punção entre o disco de bloqueio interno e externo. O vedante interno e o disco de bloqueio externo são mantidos no lugar através da fricção no veio multifilamentar. A hemóstase é alcançada por meios mecânicos. Os elementos de oclusão degradam-se por hidrólise.

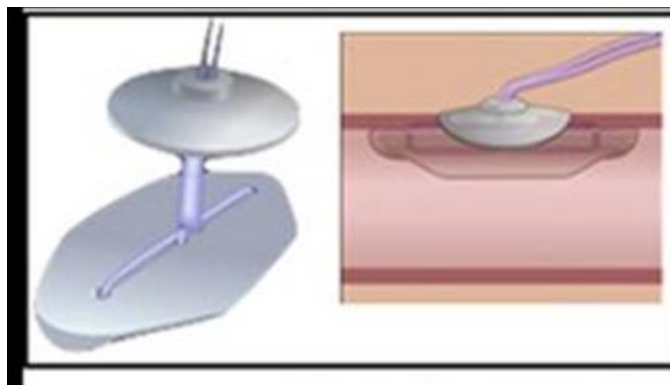
Os componentes de oclusão implantáveis, a vedação interna e o disco de bloqueio externo degradam-se em 18 (dezoito) meses, enquanto se estima que o multifilamento se degrade e seja absorvido por hidrólise pelo tecido circundante após 2 (dois) a 3 (três) anos. A capacidade dos componentes de oclusão implantáveis de manter a compressão na arteriotomia foi testada em até 8 (oito) horas. Os produtos de degradação são metabolizados e excretados na urina ou expirados

como dióxido de carbono através dos pulmões. Não foram observados efeitos de acumulação em estudos em animais. Os componentes adicionais do FemoSeal™ que entrarão em contacto com tecido vivo ou sangue durante o procedimento são a bainha do invólucro do cone, dilatador, tubo de manipulação, controlador de avanço e o fio-guia.

**Figura 1.1 Vedante interno e disco de bloqueio externo, respetivamente**

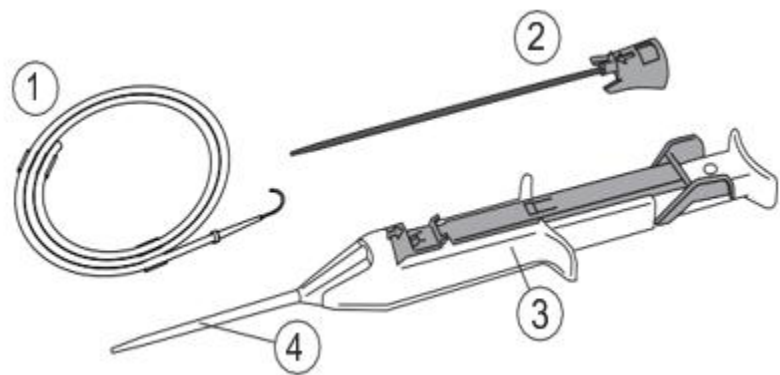


**Figura 1.2 Vedante interno e disco de bloqueio externo colocados**



A unidade FemoSeal™ é embalada juntamente com um dilatador, um fio-guia com um DE de 0,038" (0,97 mm) e 27,5" (70 cm) de comprimento e um esticador em J. Consulte a **Figura 1.3** abaixo. O fio-guia está contido dentro de um tubo de polietileno. Todas as peças são embaladas num tabuleiro de papel fixo. A embalagem também inclui o cartão de implante do paciente. O FemoSeal™ Vascular Closure System não requer acessórios adicionais para o dispositivo funcionar conforme previsto e o dispositivo destina-se apenas a ser utilizado com o dilatador e fio-guia incluídos na embalagem do produto.

**Figura 1.3 Unidade do FemoSeal™ VCS com o fio-guia e dilatador**



**1.2.2 Matérias-primas e componentes**

A **Tabela 1.1** abaixo lista os componentes do FemoSeal™ VCS.

**Tabela 1.1 Matérias-primas e componentes do FemoSeal™ VCS**

| Número de peça | Descrição                                                        |                                                            | Materiais                                                                                                                                                                                  |
|----------------|------------------------------------------------------------------|------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1              | Fio guia de 0,038" (0,97 mm) com um esticador em J para fio-guia |                                                            | Fio-guia: Aço inoxidável 304<br><br>Esticador em J: Polipropileno, pigmento roxo<br><br>Clipe: Polietileno<br><br>Tubuladuras: Polietileno                                                 |
| 2              | Dilatador FemoSeal                                               |                                                            | Canhão: Tetrahidrofurano, pigmento azul, tereftalato de polibutileno (PBT)<br><br>Tubo: Polietileno de alta densidade (HDPE), pigmento preto<br><br>Lubrificante: Silicone Dow Corning 360 |
| 3/4            | Unidade FemoSeal                                                 | Moldado RD7 – Vedante interno e disco de bloqueio externo* | Copolímero entre glicolida, carbonato de trimetileno, ε-caprolactona e TMP: trimetilolpropano (iniciador)                                                                                  |
|                |                                                                  | Multifilamento *                                           | Copolímero segmentado entre L,L-Lactideo, carbonato de trimetileno, ε-caprolactona e 1,3 propanodiol (iniciador)                                                                           |



|  |  |                             |                                                                           |
|--|--|-----------------------------|---------------------------------------------------------------------------|
|  |  |                             | O revestimento é de copolímero entre glicolida, ε-caprolactona e L-lisina |
|  |  | Tubo de manipulação         | Polipropileno                                                             |
|  |  | Empurrador                  | Aço inoxidável 304 V                                                      |
|  |  | Slider                      | Tereftalato de polibutileno (PBT)                                         |
|  |  | Invólucro                   | Tereftalato de polibutileno (PBT)                                         |
|  |  | Botão                       | Tereftalato de polibutileno (PBT)                                         |
|  |  | Tampa do botão              | Copolímero de polioximetileno (POM)/poliacetal                            |
|  |  | Manga                       | Tereftalato de polibutileno (PBT)                                         |
|  |  | Espaçador                   | Tereftalato de polibutileno (PBT)                                         |
|  |  | Cone                        | Polipropileno                                                             |
|  |  | Tampa do invólucro          | Tereftalato de polibutileno (PBT)                                         |
|  |  | Trinco de segurança         | Tereftalato de polibutileno (PBT), pigmento azul                          |
|  |  | Tampa da manga              | Tereftalato de polibutileno (PBT)                                         |
|  |  | Junta do tubo               | Base de silicone A 70                                                     |
|  |  | Junta do invólucro          | Base de silicone A 50                                                     |
|  |  | Mola                        | Aço inoxidável 302                                                        |
|  |  | Bainha do invólucro do cone | Polipropileno<br>Silicone Dow Corning 360, Hexano                         |

\* Parte implantável do dispositivo; os componentes implantáveis são seguros em RM

O FemoSeal™ VCS é esterilizado por óxido de etileno (EO) e é um dispositivo médico de utilização única. O dispositivo FemoSeal™ VCS foi concebido de forma a não poder ser reutilizado.

### **Modo de atuação**

O FemoSeal™ VCS promove a hemóstase mecânica através da colocação de elementos de oclusão implantáveis dentro e fora da artéria femoral comum. O mecanismo que impede a hemorragia é fornecido pelo vedante interno que sela o local da punção e o disco de bloqueio externo que mantém o vedante interno na posição.

### 1.2.3 Benefício clínico

O FemoSeal™ VCS proporciona os seguintes benefícios clínicos em relação à oclusão vascular após punção femoral comum:

- Redução do tempo até à hemóstase<sup>1</sup>
- Redução do tempo até à deambulação<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

### 1.2.4 Geração(ões) ou variantes anteriores

- A primeira versão do FemoSeal™ VCS (n.º 11200) foi vendida no mercado europeu durante o ano 2005 e parte de 2006.
- O FemoSeal™ VCS atual (n.º 11202), com um sistema de administração melhorado, está no mercado desde 28 de março de 2006.

### 1.2.5 Acessórios que se destinam a ser utilizados em combinação com o dispositivo

A unidade FemoSeal™ é embalada em conjunto com um dilatador, um fio-guia com um DE de 0.038" (0.97 mm) e 27.5" (70 cm) de comprimento e um esticador em J. O fio-guia é um acessório da unidade FemoSeal™. O esticador em J é um componente do fio-guia, enquanto o dilatador é um componente da unidade FemoSeal™. O fio-guia é o único acessório considerado. O fio-guia está contido dentro de um tubo de polietileno. Todas as peças são embaladas num tabuleiro de papel fixo. A embalagem também inclui o cartão de implante do paciente. O FemoSeal™ Vascular Closure System não requer acessórios adicionais para o dispositivo funcionar conforme previsto e o dispositivo destina-se apenas a ser utilizado com o dilatador e fio-guia incluídos na embalagem do produto.

### 1.2.6 Outros dispositivos e produtos destinados à utilização em combinação com o dispositivo

O FemoSeal™ VCS não requer dispositivos adicionais para funcionar como pretendido.

## 1.3 Riscos e avisos

### 1.3.1 Riscos residuais e efeitos indesejáveis

Os eventos adversos, lesões e complicações conhecidos ou previsíveis associados à utilização do FemoSeal™ VCS como resultado de risco residual estão listados na **Tabela 1.2**. A taxa de ocorrência baseia-se numa análise da Documentação de risco e é calculada com base em dados de Vigilância pós-comercialização de 1 de setembro de 2015 a 31 de agosto de 2024. Não

existem riscos residuais desconhecidos para o FemoSeal™ VCS e todos os riscos aplicáveis foram geridos através das Instruções de utilização e do processo de gestão de riscos.

**Tabela 1.2. Eventos adversos/complicações com o FemoSeal**

| Danos                                       | Taxa de ocorrência (%) | Fatores de mitigação                                                                                                                                                                               |
|---------------------------------------------|------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Reação alérgica                             | 0,0000                 | As ações e planos para reduzir o risco tanto quanto possível foram tidos em conta pelas características de conceção do produto, orientações de fabrico, rotulagem do produto e formação do médico. |
| Aneurisma                                   | 0,0000                 |                                                                                                                                                                                                    |
| Fístula AV                                  | 0,0001                 |                                                                                                                                                                                                    |
| Perda de sangue/hemorragia                  | 0,0280                 |                                                                                                                                                                                                    |
| Morte                                       | 0,0002                 |                                                                                                                                                                                                    |
| Equimose                                    | 0,0000                 |                                                                                                                                                                                                    |
| Embolia                                     | 0,0000                 |                                                                                                                                                                                                    |
| Reação a corpo estranho                     | 0,0000                 |                                                                                                                                                                                                    |
| Hematoma                                    | 0,0027                 |                                                                                                                                                                                                    |
| Hemorragia                                  | 0,0001                 |                                                                                                                                                                                                    |
| Infeção                                     | 0,0002                 |                                                                                                                                                                                                    |
| Reação inflamatória                         | 0,0000                 |                                                                                                                                                                                                    |
| Dormência                                   | 0,0000                 |                                                                                                                                                                                                    |
| Dor                                         | 0,0000                 |                                                                                                                                                                                                    |
| Desconforto do paciente                     | 0,0004                 |                                                                                                                                                                                                    |
| Atraso no procedimento                      | 0,0065                 |                                                                                                                                                                                                    |
| Pseudoaneurisma                             | 0,0004                 |                                                                                                                                                                                                    |
| Hemorragia retroperitoneal                  | 0,0002                 |                                                                                                                                                                                                    |
| Sépsis                                      | 0,0000                 |                                                                                                                                                                                                    |
| Tromboembolia                               | 0,0000                 |                                                                                                                                                                                                    |
| Trombose                                    | 0,0001                 |                                                                                                                                                                                                    |
| Oclusão do vaso/isquemia do membro inferior | 0,0002                 |                                                                                                                                                                                                    |
| Perfuração do vaso                          | 0,0000                 |                                                                                                                                                                                                    |
| Dissecção/laceração de tecido vascular      | 0,0003                 |                                                                                                                                                                                                    |

### 1.3.2 Avisos e precauções

#### Avisos

1. Não utilizar se a embalagem estiver danificada ou se qualquer barreira estéril não estiver intacta.
2. Não utilizar após o prazo de validade – os componentes biodegradáveis podem não ter um desempenho adequado.
3. Não utilizar se algum dos artigos parecer estar danificado ou defeituoso de qualquer forma.
4. A utilização do FemoSeal™ Vascular Closure System nos casos em que possa ter ocorrido a contaminação bacteriana da bainha de procedimento ou do tecido circundante, pode causar infeção.
5. Caso se suspeite que tenha ocorrido a punção da parede arterial posterior ou que tenha sido feita mais de uma punção arterial, não se deve depender apenas do FemoSeal™ Vascular Closure System para alcançar a hemóstase arterial. Utilizar compressão manual ou mecânica adicional.
6. Se o local de punção se encontrar na bifurcação da artéria femoral, ou distal à mesma, o FemoSeal™ Vascular Closure System não deve ser utilizado devido ao risco de posicionamento incorreto do vedante interno. Este evento pode resultar em complicações hemorrágicas e/ou perturbação do fluxo sanguíneo normal.
7. Se ocorrer uma hemorragia arterial persistente no local da incisão, não cortar o multifilamento até à obtenção de hemóstase. Caso não se obtenha hemóstase, fixar o multifilamento com um penso esterilizado e aplicar compressão suplementar até à obtenção de hemóstase. No caso de hemorragia arterial persistente, podem ocorrer complicações hemorrágicas significativas que podem resultar em lesões no paciente ou na morte.
8. Não utilizar o FemoSeal™ Vascular Closure System se o local de punção for proximal ao ligamento inguinal, pois tal pode resultar num hematoma retroperitoneal.
9. Os pacientes com um risco mais elevado de hemorragia podem sofrer um aumento da perda de sangue, exigindo uma transfusão.
10. Se o disco interno se soltar, pode causar um evento trombótico e/ou embólico.

#### Precauções

1. O procedimento de colocação do FemoSeal™ Vascular Closure System deve ser realizado por médicos com formação adequada na utilização do dispositivo.
2. Realizar um angiograma femoral limitado ou uma punção femoral orientada por ecografia antes da colocação do FemoSeal™ Vascular Closure System.

3. Interromper o procedimento em caso de:
  - Diâmetro do lúmen da artéria femoral comum < 5 mm.
  - Estenose e/ou presença significativa de placa próximo do local de punção femoral arterial comum.
  - A punção arterial é efetuada na bifurcação da artéria femoral, ou é distal à mesma.
  - Presença de ramificações anómalas ou anomalias dos vasos próximo do local de punção femoral comum.
4. Na presença de hematomas, deve tomar-se especial cuidado para inserir a bainha do invólucro do cone corretamente na artéria.
5. Utilizar uma técnica de punção de parede única. Não puncionar a parede posterior da artéria.
6. Seguir sempre uma técnica estéril ao utilizar o FemoSeal™ Vascular Closure System.
7. O FemoSeal™ Vascular Closure System destina-se a uma única utilização e não deve ser re-esterilizado nem reutilizado. A unidade FemoSeal™ foi concebida de forma a não poder ser reutilizada.
8. Se a colocação do vedante interno encontrar resistência inesperada, interromper o procedimento.
9. Para uma colocação correta do vedante interno, reposicionar o polegar de modo a que o botão possa voltar para trás livremente.
10. Certificar-se de que a ponta da bainha do invólucro do cone da unidade FemoSeal™ está sob a superfície da pele antes da colocação do disco de bloqueio externo. O disco de bloqueio externo pode ser colocado inadvertidamente acima do nível da pele em pacientes com uma distância curta entre a artéria femoral e o nível da pele.
11. Para uma colocação correta, pode ser necessária uma incisão cutânea antes da colocação.
12. Se o vedante interno estiver dentro da artéria, mas não for possível premir totalmente o botão e colocar o disco de bloqueio externo, poderá ser necessária uma cirurgia para remover os elementos de oclusão FemoSeal™.
13. Se for necessária a repunção da mesma artéria femoral no prazo de 18 meses, esta deve ser feita no mínimo a um centímetro proximal ao local de acesso anterior do FemoSeal™ Vascular Closure System.
14. Instruir o paciente para seguir as indicações do médico relativamente à inspeção do local de oclusão.

15. Instruir o paciente a ter consigo a Ficha de informações para o paciente durante os 18 meses seguintes

**Precauções aquando da alta**

Antes de se considerar dar alta ao paciente, avaliá-lo quanto às seguintes condições clínicas:

- 1. Hemorragia e/ou hematoma no local de oclusão.
- 2. Dor ao caminhar.
- 3. Sinais de infeção no local de oclusão.

**1.3.3 Ações corretivas de segurança no local**

Foi realizada uma Ação corretiva de segurança no local envolvendo o FemoSeal™ VCS durante o período de 1 de setembro de 2019 a 31 de agosto de 2024.

Em 2022, a Terumo retirou voluntariamente o FemoSeal™ VCS devido a reclamações alegando as falhas no processo e nos testes de lançamento de lote do produto FemoSeal fabricado pela Elkton para medição da força de compressão e força de retração. Foi recolhido um total de 950 unidades na Coreia do Sul.

**1.4 Avaliação clínica e acompanhamento clínico pós-comercialização**

A **Tabela 1.3** inclui uma lista de estudos piloto incluídos para colocar o FemoSeal™ VCS no mercado, bem como estudos pós-comercialização e atividades de acompanhamento clínico pós-comercialização. A versão do dispositivo utilizada no estudo está incluída na tabela abaixo. A primeira versão do FemoSeal™ VCS (n.º 11200) esteve no mercado até 2006, enquanto a versão seguinte (n.º C11202) foi lançada no mercado em 2006 e é a que está no mercado atualmente.

**Tabela 1.3 Resumo de estudos piloto**

| Testes funcionais pré-comercialização em animais                                                                                                                                                                                                                        | Versão do dispositivo |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                 |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                 |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                 |
| <b>Primeiro estudo clínico em humanos</b>                                                                                                                                                                                                                               |                       |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                 |

| Estudos clínicos pós-comercialização concluídos                                                                                 |                               |
|---------------------------------------------------------------------------------------------------------------------------------|-------------------------------|
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                      | C11202<br>(dispositivo atual) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                               | C11202<br>(dispositivo atual) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | C11202<br>(dispositivo atual) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)          | C11202<br>(dispositivo atual) |
| Estudos clínicos pós-comercialização planejados/em curso                                                                        |                               |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                      | C11202<br>(dispositivo atual) |
| Atividades de acompanhamento clínico pós-comercialização                                                                        |                               |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(dispositivo atual) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(dispositivo atual) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(dispositivo atual) |

#### 1.4.1 Resumo de dados de (investigações clínicas e testes em animais) pré-comercialização

A Tabela 1.4 abaixo descreve todos os estudos pré-comercialização, tanto de testes em animais como de investigações clínicas.

**Tabela 1.4 Resumos de estudos pré-comercialização**

| Testes funcionais pré-comercialização em animais                                                                              |                                |                                              |                                                                                                                                                       |                                                                                                                                                        |                                                                                                                                                                                      |
|-------------------------------------------------------------------------------------------------------------------------------|--------------------------------|----------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Nome do estudo                                                                                                                | Ano/CI                         | Tipo de estudo                               | Objetivos                                                                                                                                             | Marcos                                                                                                                                                 | Crítérios de aceitação potencial                                                                                                                                                     |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional | 2000<br>Radi Medical System AB | Estudo em animais; investigação exploratória | O objetivo do estudo foi avaliar a biocompatibilidade e biofuncionalidade de um implante biodegradável concebido para alcançar a hemóstase no sistema | N = 3 ovelhas adultas, 1 animal por ponto temporal<br><br>Acompanhamento para análise histopatológica, gradação macroscópica e análise ultraestrutural | Patência arterial<br>• Avaliação do fluxo sanguíneo pós-colocação – 2/3 de redução do fluxo sanguíneo associada a vasoespasmo arterial temporário que foi atribuído ao procedimento, |

|                                                                                                                                           |                                  |  |                                                                                                          |                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|-------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|--|----------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | Realizado pela Biomatech, França |  | vascular. O relatório aborda animais de reserva a partir do número de estudo 862 (Documento n.º 1051-01) | <ul style="list-style-type: none"> <li>12 meses</li> <li>15 meses</li> <li>18 meses</li> </ul> <p>Acompanhamento ecográfico com doppler a cores – 30 dias nos locais de acesso arterial femoral e carótida</p> | <p>ambos ocorreram na artéria carótida comum esquerda</p> <p>Avaliação ecográfica com doppler a cores (4 semanas) – 3/3 (100%) sem redução significativa do fluxo sanguíneo 30 dias após a implantação</p> <p>Observações macroscópicas</p> <ul style="list-style-type: none"> <li>12 meses – patência confirmada macroscopicamente pela ausência de oclusão anatomicamente visível; sem lesões macroscópicas de intolerância local (hemorragia, necrose ou neovascularização); o encapsulamento do disco interno pareceu ser marcado</li> <li>15 meses – a observação macroscópica não mostrou sinais de inflamação; não foram identificados nenhuns resíduos dos discos internos ou externos; o tecido encapsulado localizado na área do disco externo parecia o mesmo que na observação de 12 meses</li> <li>18 meses – a observação macroscópica não apresentou sinais de intolerância local, disco externo visível (3/3 casos), degradação do disco interno completo; 1/3 (artéria carótida comum esquerda) – depressão da parede arterial observada no local do implante (pode estar relacionada com a colocação do dispositivo)</li> </ul> <p>Conclusões</p> <ul style="list-style-type: none"> <li>Macroscopicamente, 12, 15 e 18 meses após a implantação, não foram detetados sinais necróticos, degenerativos ou trombóticos.</li> <li>O processo de degradação dos discos internos e externos parecia progredir entre 12 e 18 meses e ficar completo após 18 meses, com um tecido esbranquiçado a cobrir a área implantada.</li> <li>Histologicamente, após 18 meses, o material</li> </ul> |
|-------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|--|----------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|



|                                                                                                                                                                                                                                                                         |                                                                     |                                              |                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------|----------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                                                                                         |                                                                     |                                              |                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                | polimérico já não era visível, mas estava presente um tecido fibroso endoluminal. Não foram observadas lesões necróticas, degenerativas ou trombóticas.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 2002 Radi Medical System AB<br><br>Realizado pela Biomatech, França | Estudo em animais; investigação exploratória | O objetivo do estudo foi avaliar a biocompatibilidade de um implante biodegradável destinado a alcançar a hemóstase no sistema vascular. | Acompanhamento (após a implantação) <ul style="list-style-type: none"> <li>12 semanas</li> <li>24 semanas</li> <li>36 semanas</li> </ul> N = 12 ovelhas, 3 animais por ponto temporal, 3 animais reservados sacrificados aos 12, 15 e 18 meses<br><br>Locais de implantação – artérias femorais direita e esquerda, artérias carótidas comuns direita e esquerda<br><br>Análise ecográfica com doppler a cores | <u>Patência das artérias carótidas e femorais após 4 semanas</u> <ul style="list-style-type: none"> <li>Redução significativa do fluxo sanguíneo 0/12 (0%)</li> </ul> <u>Sem redução significativa do fluxo sanguíneo</u> <ul style="list-style-type: none"> <li>Inibição grave do fluxo sanguíneo relacionada com a inserção do dispositivo 0/12 (0%)</li> <li>Redução do fluxo sanguíneo na carótida comum esquerda 2/12 (16,6%) devido a vasoespasmos arterial temporário (atribuído a cirurgia, não a dispositivo)</li> </ul> <u>Inibição do fluxo sanguíneo por acompanhamento</u> 12 semanas – 0/12 (0%)<br>24 semanas – 0/12 (0%)<br>36 semanas – 0/12 (0%)<br><br>Medições da tensão arterial (3 ovelhas – 36 semanas) <ul style="list-style-type: none"> <li>Não foi detetada uma redução significativa do fluxo sanguíneo</li> </ul> Dados macroscópicos para integração e degradação (Grau 0-4)<br><br><u>Acessos carotídeos</u><br><u>Lado interno</u> - encapsulamento<br>12 semanas 1,3<br>24 semanas 0,8<br>36 semanas 0,7<br>- degradação do material<br>12 semanas 2,2<br>24 semanas 2,3<br>36 semanas 0,7<br><u>Lado externo</u> |

|  |  |  |  |  | - encapsulamento<br>12 semanas 2,0<br>24 semanas 1,0<br>36 semanas 0,8<br>- degradação do material<br>12 semanas 2,0<br>24 semanas 2,7<br>36 semanas 3,2<br><br><u>Locais femorais</u><br><u>Lado externo</u><br>- encapsulamento<br>12 semanas 1,0<br>24 semanas 2,7<br>36 semanas 1,0<br>- degradação do material<br>12 semanas 2,0<br>24 semanas 2,4<br>36 semanas 3,0<br><br><u>Lado interno</u><br>- encapsulamento<br>12 semanas 2,0<br>24 semanas 1,2<br>36 semanas 1,0<br>- degradação do material<br>12 semanas 1,0<br>24 semanas 2,2<br>36 semanas 3,0<br><br><u>Dados histológicos para</u><br><u>integração, degradação e</u><br><u>parâmetros inflamatórios (média</u><br><u>de valores relevantes, Índice 0-4)</u><br><u>n=6</u><br><br><u>Locais carotídeos</u><br>Fibrose externa<br>12 semanas – 2,3<br>24 semanas – 2,3<br>36 semanas – 1,8<br>Neointima interna<br>12 semanas – 3,0<br>24 semanas – 2,7<br>36 semanas – 3,3<br>Degradação do material<br>12 semanas – 1,7<br>24 semanas – 3,0<br>36 semanas – 3 +<br>Parâmetros inflamatórios<br>(macrófagos) |
|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | 12 semanas – 3,0<br>24 semanas – 1,7<br>36 semanas – 1,7<br><u>Locais femorais</u><br>Fibrose externa<br>12 semanas – 1,3<br>24 semanas – 1,5<br>36 semanas – 1,7<br>Neointima interna<br>12 semanas – 3,7<br>24 semanas – 3,3<br>36 semanas – 3,8<br>Degradação do material<br>12 semanas – 2,0<br>24 semanas – 3,0<br>36 semanas – 3 +<br>Parâmetros inflamatórios<br>(macrofagos)<br>12 semanas – 3,5<br>24 semanas – 1,8<br>36 semanas – 1,8<br><br><u>Valores de patência<br/> histomorfológica</u><br>Locais carotídeos<br>12 semanas 74,0%<br>24 semanas 81,9%<br>36 semanas -89,43%<br>Locais femorais<br>12 semanas – 42,2%<br>24 semanas – 73,21%<br>36 semanas – 78,71%<br><br><u>Patência do vaso US (média %)</u><br>Local carotídeo<br>12 semanas 94,6%<br>24 semanas – 96,7%<br>36 semanas – 94,7%<br>Locais femorais<br>12 semanas – 66,9%<br>24 semanas – 63,6%<br>36 semanas – 75,1%<br><br>Conclusões <ul style="list-style-type: none"> <li>Não foi detetado qualquer sinal de intolerância local significativo (ausência de lesões inflamatórias, necróticas ou degenerativas visíveis) às 12, 24 ou 36 semanas</li> </ul> |
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|                                                                                                                                                                                                                                                                      |                                                                                 |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                            | <ul style="list-style-type: none"> <li>Não foi registada qualquer reação tissular adversa significativa em relação ao hospedeiro e dispositivo</li> <li>A degradação do implante estava quase concluída às 36 semanas</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomech, France).</p> | <p>2002</p> <p>Radi Medical System AB</p> <p>Realizado pela Biomech, França</p> | <p>Estudo em animais</p> | <p>A finalidade do estudo foi avaliar a biocompatibilidade e biofuncionalidade de um implante biodegradável concebido para alcançar a hemóstase no sistema vascular. O dispositivo testado destinava-se a entrar no orifício de punção nas artérias para alcançar a hemóstase. Um disco entrou no orifício de punção na artéria e o outro apertava o disco interno a partir do externo da artéria. Ambos os discos foram inseridos através de uma bainha introdutora. Os discos foram concebidos para evitar hemorragias, sarar para a parede do vaso e, por fim, degradar-se e ser absorvidos. O estudo foi concebido para recolher e analisar dados após a implantação funcional na ovelha e no porco para avaliar a capacidade do implante para manter a função fisiológica quando utilizado no sistema circulatório, para determinar a resposta do hospedeiro e a resposta do dispositivo (integridade física, encapsulamento tissular no sacrifício) e para avaliar a degradação do implante</p> | <p>O período/acompanhamento de implantação é de 5 semanas para todos os animais</p> <p>4 ovelhas, 1 porco</p> <p>14 elementos de oclusão</p> <p>8 elementos de oclusão implantados em 2 ovelhas,</p> <p>2 elementos de oclusão implantados em 1 porco</p> <p>Quando dois elementos de oclusão foram implantados na mesma artéria femoral, foram implantados a uma distância &gt; 30 mm</p> | <p>Foram registados todos os critérios de sinais adversos (inflamação, necrose, hemorragia ou qualquer outra lesão) ou todas as formações finas de camadas pseudo-intimais. Foi dedicada especial atenção à integração tissular inicial do dispositivo, com especial ênfase no encapsulamento do disco interno.</p> <p>Macroscopicamente, não foram observados sinais significativos de intolerância local ou formação de trombos. A observação macroscópica não revelou qualquer diferença entre o ovelha e o porco após a implantação dos elementos de oclusão nas artérias femorais.</p> <p>Macroscopicamente, não foram observados sinais significativos de intolerância local ou formação de trombos. A observação macroscópica não revelou qualquer diferença entre o ovelha e o porco após a implantação dos elementos de oclusão nas artérias femorais.</p> <p>A análise histopatológica do local de implantação nas ovelhas não demonstrou quaisquer reações adversas locais. Os discos internos e externos mostraram sinais de degradação e, em alguns</p> |

|                                                                                                                                                                                          |                              |                                                |                                                                                                                                                                                                                                        |                                                                                                                                                       | <p>casos, estavam divididos em peças mais pequenas. Os discos internos foram completamente integrados no tecido neointimal. No porco, a análise histopatológica mostrou sinais ligeiramente mais inflamatórios à volta dos discos internos e externos. Em ambos os animais, o multifilamento apresentava sinais ligeiramente mais inflamatórios do que no material do disco, o que é normal para suturas entrançadas devido à maior área de superfície.</p> <p>A patência do vaso foi medida ao fim de 5 semanas utilizando três métodos diferentes: histomorfométrico e histomorfométrico em combinação com a medição do diâmetro do vaso utilizando um calibrador e utilizando uma ecografia com doppler colorido. A patência média dos vasos nas ovelhas situava-se entre 60 e 80%, dependendo do método (12 observações). No porco, a patência média do vaso situava-se entre 40 e 80% (2 observações).</p> |
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| <b>Primeiro estudo clínico em humanos</b>                                                                                                                                                |                              |                                                |                                                                                                                                                                                                                                        |                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Nome do estudo                                                                                                                                                                           | Ano/CI                       | Tipo de estudo                                 | Objetivos                                                                                                                                                                                                                              | Marcos                                                                                                                                                | Critérios de aceitação potencial                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi | 2004 Radi Medical Systems AB | Teste aberto, de segmento único, multicêntrico | Os objetivos do estudo foram determinar a segurança, o desempenho e a eficácia do FemoSeal Vascular Closure System (Sistema FemoSeal) em geral, e especificamente dos elementos de oclusão, em pacientes submetidos a procedimentos de | Estudo de 2 partes<br><br>Total n = 80<br>Parte 1 n = 20<br>Parte 2 n = 60<br>Indicações:<br>Parte 1 – diagnosticar a cateterização cardíaca usando a | Resultados<br>- <u>hemóstase alcançada com FS sem compressão</u><br>- Parte 1 20/20 (100%)<br>- Parte 2 58/60 (97%)<br>Tempo mediano até à hemóstase no momento do procedimento (parte 2) – 1,0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |

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| Medical Systems AB. |  |  | diagnóstico cardíaco ou cardiologia intervencional utilizando acesso à artéria femoral. | artéria femoral como local de acesso<br><br>Parte 2 – pacientes submetidos a procedimentos de diagnóstico e cirúrgicos cardíacos utilizando a artéria femoral como local de acesso<br><br>Acompanhamento de 30 dias | <p>minutos (intervalo imediato – 8 minutos)</p> <p><u>Tempo até à deambulação (minutos)</u></p> <p>Parte 1 –<br/>Mediana: 33,0<br/>média: 67,8</p> <p>Parte 2 –<br/>mediana: 45<br/>média: 87,5</p> <p><u>Incidência de complicações vasculares graves – acompanhamento de 30 dias</u></p> <p>Parte 1<br/>- Sem complicações vasculares 20/20 (100%)</p> <p>Parte 2<br/>Pseudoaneurisma - 1/59 (1,69%)</p> <p><u>Insucesso do tratamento</u></p> <p>Parte 1 – 0/20 (0%)<br/>Parte 2 – 3/60 (5%)</p> <ul style="list-style-type: none"> <li>• 2 devido a não ter sido possível alcançar a hemóstase sem utilização de compressão</li> <li>• 1 devido a uma complicação vascular grave, pseudoaneurisma</li> </ul> <p><u>Exsudação persistente</u></p> <p>Parte 1 – 0/20 (0%)<br/>Parte 2 – 8/60 (13%)</p> <p><u>Hematoma</u></p> <p>Parte 1 – 0/20 (0%)<br/>Parte 2 – 6/60 (10%)</p> |
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Como parte do plano de desenvolvimento pré-comercialização para o FemoSeal™ VCS, foram realizados três testes funcionais em animais. Em 2000, antes de iniciar estudos clínicos, foi realizado um estudo em animais para avaliar a biofuncionalidade do FemoSeal™ VCS. Este estudo avaliou a capacidade dos elementos de oclusão para manter a função fisiológica e avaliar a sua degradação. Aos 18 meses, o material do disco interno e externo já não era visível, tendo sido substituído por um tecido fibroso endoluminal. Concluindo, foi confirmada a capacidade do elemento de oclusão do FemoSeal™ VCS de manter a função fisiológica quando utilizado no sistema circulatório.

Em 2002, foi realizado um estudo em animais para avaliar a biocompatibilidade e biofuncionalidade de um implante biodegradável, o FemoSeal™ VCS, concebido para alcançar a hemóstase no sistema vascular. Em resumo, a degradação do implante estava quase concluída ao fim de 36 semanas e não houve uma reação tissular adversa significativa.

Outro estudo realizado em 2002 avaliou a biocompatibilidade e biofuncionalidade de um implante biodegradável, o FemoSeal™ VCS, concebido para alcançar a hemóstase no sistema vascular. Após 5 semanas, o encapsulamento do disco estava completo e foram observados sinais de degradação nos discos internos e externos. Concluindo, foi confirmada a capacidade do implante para manter a função fisiológica quando utilizado no sistema circulatório.

Como parte do plano de desenvolvimento clínico para o FemoSeal™ VCS, a Radi Medical System AB realizou uma investigação clínica pré-comercialização. Esta investigação clínica não foi publicada nem está disponível online. O estudo com o modelo de dispositivo n.º 11200 foi realizado em 2002-2004 ao abrigo da Norma Europeia EN 540 (Investigação Clínica de Dispositivos Médicos para Sujeitos Humanos) e em conformidade com as Considerações Gerais do ICH para Ensaio Clínicos e Diretrizes para Boas Práticas Clínicas. Os detalhes deste estudo estão documentados no relatório EU-SE-001. O ensaio clínico foi documentado no Relatório Final da Radi Medical Systems AB, "Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures". O estudo clínico foi realizado com o primeiro modelo n.º 11200 do FemoSeal e centrou-se na segurança e eficácia dos componentes de oclusão implantáveis. A única diferença entre o primeiro modelo n.º 11200 e o modelo atual, o C11202, é o tamanho francês, 6F e 7F respetivamente, e o sistema de entrega melhorado. Os benefícios clínicos, a utilização prevista, os princípios de funcionamento e as matérias-primas dos elementos de oclusão implantáveis, a vedação interna e o disco de bloqueio externo permanecem inalterados.

A utilização prevista do dispositivo era para pacientes submetidos a procedimentos de diagnóstico ou cirúrgicos cardíacos utilizando a artéria femoral como ponto de acesso. O objetivo deste estudo foi determinar a segurança, desempenho e eficácia do FemoSeal™ VCS. Este foi um estudo prospetivo, multicêntrico, aberto de segmento único com acompanhamento de 30 dias.

O parâmetro de desempenho primário foi o tempo até à hemóstase definida como a ausência de hemorragias bruscas. O parâmetro de segurança primário foi a incidência de complicações vasculares significativas ao longo de 30 dias. Os parâmetros secundários incluíram tempo até à deambulação, a proporção de insucesso no tratamento, incidência de eventos adversos e características de desempenho do dispositivo durante a administração e colocação.

Os pacientes incluídos neste estudo foram adultos capazes de dar consentimento informado e com pelo menos um pulso podal intacto. Os pacientes foram excluídos do estudo se apresentaram alguma das seguintes condições:

- Histórico de doença vascular periférica
- Doença autoimune
- Doença hemorrágica conhecida de anemia grave
- INR >1,5
- Enfarte do miocárdio com 72 horas
- Hipertensão não controlada apesar do tratamento
- Obesidade impedindo o acesso com técnica de Seldinger
- Presença de enxerto vascular ou stent no local da arteriotomia
- Punção ipsilateral anterior no prazo de 3 meses
- Esperança de vida < 6 meses

Adicionalmente, os pacientes foram examinados intraoperatoriamente e excluídos do estudo se alguma das seguintes condições foi observada:

- Diâmetro do lúmen da artéria femoral comum <5 mm
- Ramificações arteriais dentro de 2 cm proximais ao local da punção
- Estenose significativa dentro de 3 cm do local de punção
- Utilização da bainha introdutora primária >6Fr
- Punção na bifurcação femoral ou distal
- Punções femorais múltiplas
- Punção da parede femoral posterior conhecida ou suspeita
- Hematoma grande (2,6 cm) após a conclusão do procedimento
- Dificuldade na inserção da bainha primária para o procedimento devido a tecido ou vaso tortuoso



Este estudo de protocolo único foi realizado em duas partes: 20 pacientes foram inscritos durante a Parte 1, depois foi concluída uma análise de segurança, e depois foram inscritos mais 60 pacientes durante a Parte 2.

Na Parte 1, a média de idades dos pacientes inscritos era de 65,9 anos, 70,0% dos pacientes eram homens e 95% dos pacientes estavam a tomar medicação concomitante. Na Parte 2 do estudo, a média de idades era de 63,8 anos, 78% eram homens e 100% estavam a tomar medicação concomitante.

Os pacientes submetidos a procedimentos de diagnóstico (Parte 1 e Parte 2) ou cirúrgicos (Parte 2) de cateterização cardíaca foram elegíveis para inscrição no estudo. Os procedimentos estavam em conformidade com o padrão de cuidados em cada um dos hospitais inscritos, seguidos da utilização do FemoSeal™ VCS. Os dados dos pacientes foram recolhidos na linha de base, durante o procedimento e 1 dia e 30 dias após o procedimento. Os resultados estão resumidos na **Tabela 1.5** e indicam que o FemoSeal™ VCS é seguro e eficaz para utilização nesta população de pacientes.

**Tabela 1.5 Resultados clínicos comunicados no estudo pré-comercialização**

|                                                                                                                            | Parte 1      | Parte 2                   |
|----------------------------------------------------------------------------------------------------------------------------|--------------|---------------------------|
| Número de pacientes                                                                                                        | 20           | 60                        |
| Tempo médio até à hemóstase                                                                                                | 1,2 minutos  | 1,6 minutos <sup>a</sup>  |
| Tempo médio até à deambulação                                                                                              | 72,2 minutos | 87,5 minutos <sup>b</sup> |
| Incidência de complicações vasculares graves <sup>c</sup>                                                                  | 0 (0%)       | 1 (2%)                    |
| Número de pacientes com eventos adversos                                                                                   | 5 (25%)      | 19 (32%)                  |
| Insucesso do tratamento (definido como complicações vasculares significativas, necessidade de compressão manual, ou ambas) | 0 (0%)       | 3 (5%)                    |
| Avarias do dispositivo                                                                                                     | 0 (0%)       | 6 (10%)                   |

<sup>a</sup>Com base no tamanho total da amostra de 58 porque 2 pacientes não alcançaram a hemóstase no momento do procedimento devido a punções ipsilaterais anteriores. A hemóstase foi alcançada aos 7 minutos e 37 minutos para estes pacientes.

<sup>b</sup>Com base no tamanho total da amostra de 59: 1 paciente não foi incluído porque foi colocado no ventilador devido a edema pulmonar e a deambulação não foi possível durante mais de uma semana.

<sup>c</sup>Definida como complicação vascular exigindo transfusão de sangue ou reparação cirúrgica, ou infeção local exigindo administração de antibiótico, hospitalização ou extensão de hospitalização, ou desbridamento do local

Não foram observadas complicações vasculares importantes na Parte 1 do estudo. Foi relatada uma complicação vascular significativa na Parte 2 do estudo: pseudoaneurisma que foi reportado no prazo de um dia após o procedimento. O evento exigia uma compressão orientada por ecografia e uma injeção de trombina no pseudoaneurisma e prolongou a hospitalização do paciente.

Dos cinco eventos adversos comunicados na Parte 1 do estudo, ocorreu um evento adverso possivelmente relacionado com o dispositivo: um evento não grave de hemorragia brusca no dia 1 após o procedimento. Dos 19 eventos adversos comunicados na Parte 2 do estudo, foram observados três eventos adversos não graves de hematoma relacionados com o dispositivo e foram observados seis eventos não graves possivelmente relacionados com o dispositivo, incluindo três relatórios de exsudação persistente, dois hematomas e uma dor na perna após exercício.

Houve 3 doentes na Parte 2 considerados falhas de tratamento: 2 devido à falha em alcançar a hemóstase sem a utilização de compressão e 1 devido à complicação vascular maior (pseudoaneurisma). Não houve insucessos do tratamento na Parte 1 do estudo.

Dos seis maus funcionamentos do dispositivo na Parte 2 do estudo, três não interferiram com a intervenção, um foi atribuído a erro do utilizador, um foi fuga no introdutor e um foi uma articulação de filamento quebrada. As duas últimas questões foram tratadas com atualizações de modelos implementadas no C11202.

A parte 2 do estudo clínico pré-comercialização não reportou os resultados do acompanhamento aos 6 meses devido à não conformidade dos pacientes. Os resultados de 30 dias do estudo clínico pré-comercialização (EU-SE-001), que está em linha com o período de tempo de acompanhamento da literatura clínica, demonstram que o FemoSeal™ VCS é seguro e eficaz.

#### 1.4.2 Resumo de dados de estudos clínicos pós-comercialização

Existiam 4 estudos clínicos pós-comercialização concluídos, descritos na **Tabela 1.6** abaixo. Estas investigações clínicas não estão publicadas nem estão disponíveis online.

**Tabela 1.6 Estudos clínicos pós-comercialização**

| Estudos clínicos pós-comercialização concluídos                                             |              |                                                                           |                                                                                                                                                                                                           |                                                                                                                                                                                     |                                                                                                                                              |
|---------------------------------------------------------------------------------------------|--------------|---------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|
| Nome do estudo                                                                              | Ano/CI       | Tipo de estudo                                                            | Objetivos                                                                                                                                                                                                 | Marcos                                                                                                                                                                              | Crítérios de aceitação potencial                                                                                                             |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI | Estudo pós-comercialização, aceitação de embalagens novas pelo utilizador | Estudo pós-comercialização realizado sobre a atualização do modelo do FemoSeal Vascular® Closure System n.º 11202 que tem um sistema de administração modificado em comparação com o primeiro modelo, n.º | 100 pacientes <ul style="list-style-type: none"><li>63 homens/37 mulheres</li><li>Idade média de 68 anos para mulheres, 65 anos para homens</li></ul> 2 hospitais suecos, 6 médicos | Resultados<br>1. Ilustrações/Instruções nas Instruções de Utilização consideradas informativas e adequadas<br>2. Hemóstase imediata (91/100) |

|                                                                                   |                                                                    |                                              |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
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|                                                                                   |                                                                    |                                              | <p>11200, para documentar a funcionalidade.</p> <p>O objetivo do estudo era obter feedback sobre as Instruções de Utilização (IU) revistas, o projeto de formação para médicos e enfermeiros, confirmar as avaliações efetuadas na análise de risco e dar contributos para quaisquer melhorias na qualidade do produto.</p> | <p>112 dispositivos</p> <p>Dados recolhidos nos formulários de registo do paciente (CRF)</p> <p>Tempo de observação planeado – 30 minutos a partir do momento da aplicação</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008) | Dr. Nicolas Moes<br>Universidade de Medicina de Innsbruck, Áustria | Avaliação confirmativa a pós-comercialização | <p>O objetivo deste estudo foi avaliar a segurança e o desempenho do FemoSeal® utilizado durante a rotina clínica normal em pacientes submetidos a diagnóstico de cateterização cardíaca ou procedimento cirúrgico cardíaco percutâneo realizado com uma bainha 7F.</p>                                                     | <p>50 pacientes consecutivos</p> <p>Indicação – diagnóstico ou cateterização cardíaca invasiva a partir da artéria femoral comum</p> <table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | <p>Parâmetros primários</p> <ul style="list-style-type: none"><li>Parâmetro de eficácia primário – TTH (tempo até à hemóstase) com ou sem exsudação, mas sem qualquer compressão adicional, manual ou mecânica.</li><li>Parâmetro de segurança – incidência de eventos adversos – complicações vasculares menores e graves e todos os outros eventos adversos – graves e não graves durante a duração do estudo (ou seja, até alta do paciente).</li></ul> <p>Resultados</p> <ul style="list-style-type: none"><li>Tempo médio até à hemóstase</li><li>Diagnóstico – 56,6 ± 29 segundos</li><li>Intervenção – 59,9 ± 16,2 segundos</li><li>Todos os pacientes – 57,8 ±26,3</li><li>Todos os pacientes conseguiram a deambulação sem qualquer problema após 4 horas de repouso na cama.</li></ul> <p>Resultados de segurança</p> <ul style="list-style-type: none"><li>49/50 (98%) sem complicações vasculares até à alta hospitalar</li><li>Tempo médio até à alta 2,6 dias</li><li>1/50 (2%) hemorragias menores no dia seguinte, após uma deambulação</li></ul> |
| n                                                                                 | 50                                                                 |                                              |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| men                                                                               | 35 (70%)                                                           |                                              |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| women                                                                             | 15 (30%)                                                           |                                              |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| PCI cases                                                                         | 15                                                                 |                                              |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| age (yrs)                                                                         | 62.8±11.1                                                          |                                              |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| body mass index (kg/m²)                                                           | 25.4±6.7                                                           |                                              |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| systolic BP (mmHg)                                                                | 131.2±20.9                                                         |                                              |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| diastolic BP (mmHg)                                                               | 77.9±10.6                                                          |                                              |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| diabetes mellitus                                                                 | 9 (18%)                                                            |                                              |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| arterial hypertension                                                             | 34 (68%)                                                           |                                              |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| previous coronary intervention                                                    | 13 (26%)                                                           |                                              |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| preprocedure aspirin                                                              | 50 (100%)                                                          |                                              |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| preprocedure clopidogrel                                                          | 50 (100%)                                                          |                                              |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Procedural unfractionated heparin                                                 | 15 (30%)                                                           |                                              |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Procedural abciximab                                                              | 2 (4%)                                                             |                                              |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |

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|                                                                                                                                 |                                 |                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | sem nada a assinalar no dia da angiografia                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | 2009 RADI                       | Estudo pós-comercialização                                    | <p>O estudo deve informar se os clientes/utilizadores sentiram algum problema com a embalagem nova, especialmente no lado exterior não estéril da bolsa Tuvek/PET-PE.</p> <p>O estudo também deve dar informação sobre se o médico responsável pelo tratamento vê alguma diferença nos passos de aplicação/colocação do dispositivo em comparação com os dispositivos usados anteriormente.</p> <p>O estudo também deve dar contributos para qualquer outra necessidade de melhoria da qualidade do produto.</p> | <p>25 dispositivos</p> <p>4 hospitais suecos</p> <p>16/25 (64%) dos pacientes eram pacientes com ICP com medicação anticoagulante intensa</p>                                                                                                                                                                                                                                                                                                                           | <p>Resultados</p> <ol style="list-style-type: none"> <li>Problemas relacionados com a embalagem – 21/25 (84%) aplicações foram bem sucedidas; 4/25 (16%) não foram bem sucedidas (1 – teste ao introdutor novo, 1 – disco interno passou através da arteriotomia no passo de recuo, o botão subiu e o disco externo foi colocado no canal tecidual da incisão, 2 – a hemóstase imediata não foi alcançada apesar de não haver problemas de colocação.)</li> <li>Hemóstase imediata de 19/25 (76%) pacientes</li> <li>Hemorragias 11/25 (44%) – 9/25 (36%) exsudação/hemorragia, 2/25 (8%) hematomas</li> </ol> <p>Taxa total de eventos 19%</p>                   |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022) | 2022/Terumo Medical Corporation | Prospetivo, multicêntrico, observacional, pós-comercialização | Demonstrar ainda mais a segurança e a eficácia do FemoSeal™ VCS na obtenção da hemóstase de locais de acesso da artéria femoral comum (CFA) em indivíduos reais submetidos a procedimentos endovasculares percutâneos                                                                                                                                                                                                                                                                                            | <ul style="list-style-type: none"> <li>Acompanhamento do paciente a 30 dias (<math>\pm</math> 7 dias) por visita ao hospital ou chamada telefónica.</li> <li>Registo: Dezembro de 2021 a julho de 2022.</li> <li>230 participantes inscritos submetidos a procedimentos endovasculares de diagnóstico ou de intervenção nos quais é utilizado o FemoSeal™</li> </ul> <p>3 locais europeus: França (92 pacientes), Alemanha (38 pacientes), Bélgica (100 pacientes).</p> | <ul style="list-style-type: none"> <li><b>Dados demográficos/comorbidades:</b> <ul style="list-style-type: none"> <li>Género: 161 homens (70%)/69 mulheres (30%).</li> <li>Idade média: <math>70 \pm 12</math>.</li> <li>IMC: <math>26,1 \pm 4,95</math> kg/m<sup>2</sup>.</li> <li>Hipertensão: 160 pacientes (69,6%).</li> <li>Dislipidemia: 128 (55,7%).</li> <li>Doença arterial coronária: 42 (18,3%).</li> <li>Fumador atual: 86 (37,6%).</li> <li>Ex-fumador: 66 (28,8%).</li> <li>Doença cardíaca coronária: 34 (14%).</li> <li>Enfarte do miocárdio anterior: 18 (7,8%).</li> <li>Revascularização arterial periférica: 12 (5,2%)</li> </ul> </li> </ul> |

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|  |  |  |  |  | <p>carótida e 83 (37,5%) e artéria do membro inferior.</p> <p>- Terapia antiplaquetária (na linha de base): 211 (91,7%), incluindo 21 (9,1%) terapia antiplaquetária dupla (DAPT).</p> <p>- Anticoagulação oral: 40 (17,4%) pacientes.</p> <p>• <b>Características de intervenção:</b></p> <p>- Definição: clínica interna 162 casos (70,4%), clínica externa 68 casos (29,6%).</p> <p>- Indicação predominante: claudicação 147 casos (63,9%).</p> <p>- Abordagem: 35 anterógrados (15,3%), 194 retrógrados (84,7%).</p> <p>• <b>Parâmetros primários:</b></p> <p>- A segurança combinada (livre de complicações graves do membro do local de acesso nas 6 horas seguintes ao procedimento) e o parâmetro de avaliação da eficácia (hemóstase bem-sucedida do local de punção) foram alcançados em 215/226 (95,1%) [IC 95%: 91,46; 97,55] pacientes no Conjunto de Análise Completo e 215/230 (93,5%) [IC a 95% 89,47, 96,30] no Conjunto Tratado FemoSeal™.</p> <p>- O parâmetro de avaliação da eficácia foi atingido em 219/226 (96,9%) IC [93,7, 98,7] dos pacientes.</p> <p>- Ponto final de segurança alcançado em 220/230 (95,2%) [IC de 95%: 92,15; 97,90] pacientes.</p> |
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|  |  |  |  | <p>• <b>Parâmetros secundários:</b></p> <ul style="list-style-type: none"> <li>- Ausência de complicações ligeiras no local de acesso durante seis horas após o procedimento alcançada em 225/230 (97,8%) [IC 95%: 95,00; 99,29].</li> <li>- Ausência de complicações graves e menores no local de acesso de seis horas a 30 dias após o procedimento alcançada em 219/230 (95,2%) [IC 95%: 91,60; 97,59] dos pacientes.</li> <li>- Tempo médio até à hemóstase com FemoSeal™ VCD: 0,42 (0,25; 0,50) minutos.</li> <li>- Tempo médio até à ambulância: 5,00 (4,54; 5,50) minutos.</li> <li>- Duração média da estadia no hospital: 23,98 (22,72; 25,00) horas.</li> <li>- Usabilidade do FemoSeal™ VCS: "fácil" ou "muito fácil" de implantar em 98,7% dos casos ("fácil" de implantar em 21 (9,2%), "muito fácil" de implantar em 205 (89,5%)) com pouca ou nenhuma resistência à implantação em 226 (98,3%) dos casos.</li> </ul> <p>152/230 (66,1%) dos pacientes tratados com o fio-guia incluído no kit FemoSeal™ (GW 0,038") e recomendado no FemoSeal™ sem quaisquer deficiências do dispositivo ou eventos adversos reportados.</p> |
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O estudo de 2006 foi realizado para confirmar a segurança e a eficácia do dispositivo atual com um sistema de administração melhorado e para obter feedback sobre as Instruções de Utilização e o programa de formação sobre o FemoSeal™ VCS. O estudo incluiu 100 pacientes e o parâmetro primário foi se a hemóstase foi alcançada, ou se eram necessárias compressões manuais ou mecânicas adicionais. Este estudo concluiu que a aplicação do FemoSeal™ VCS foi bem sucedida na maioria dos casos (91% alcançaram hemóstase imediata).

O estudo de 2008 inscreveu 50 pacientes para avaliar a segurança e o desempenho do FemoSeal™ VCS quando utilizado durante a rotina clínica normal em pacientes submetidos a cateterização cardíaca com uma bainha de 7 Fr. O parâmetro primário para o estudo foi recolher dados sobre o tempo até à hemóstase e o tempo até à deambulação sem compressão adicional, manual ou mecânica. Os resultados do estudo concluíram que o tempo médio até à hemóstase foi de 57.8 segundos e todos os pacientes conseguiram deambular após 4 horas de repouso na cama.

O estudo de 2009 destinou-se a avaliar a embalagem nova do FemoSeal™ VCS. Foram inscritos 25 pacientes no estudo. O parâmetro primário foi se o utilizador teve algum problema com a embalagem. Os utilizadores não notaram qualquer problema relativamente à embalagem nova do FemoSeal™ VCS. Este estudo também recolheu dados sobre o tempo até à hemóstase.

O estudo de 2022 destinava-se a recolher proativamente dados de segurança e de eficácia do FemoSeal VCS na obtenção da hemóstase de locais de acesso da artéria femoral comum (CFA) em indivíduos reais submetidos a procedimentos endovasculares percutâneos. Foram inscritos 230 pacientes no estudo. Os parâmetros primários para o registo são o sucesso do procedimento (ou seja, hemóstase do local de punção bem sucedida) e a redução de complicações graves (p. ex., lesão vascular, hemorragia relacionada com o local de acesso, infeção do local de acesso, compressão manual repetida e isquemia aguda ipsilateral da perna relacionada com o local do acesso novo). O estudo concluiu que o FemoSeal™ VCS tem um bom desempenho em ambientes reais e proporciona uma hemóstase eficaz e baixas taxas de complicações no local de acesso para pacientes submetidos a intervenções endovasculares periféricas. Demonstra um bom desempenho com um tempo curto até à hemóstase e um bom feedback de usabilidade para o operador, o que faz do FemoSeal™ VCS um dispositivo valioso para o fecho do acesso femoral.

### **1.4.3 Resumo de dados de acompanhamento clínico pós-comercialização**

#### **1.4.3.1 Acompanhamento clínico pós-comercialização concluído**

Na **Tabela 1.7** abaixo é descrito um resumo das atividades de acompanhamento clínico pós-comercialização concluídas.

**Tabela 1.7. Atividades de acompanhamento clínico pós-comercialização**

| Atividades de acompanhamento clínico pós-comercialização concluídas       |             |                                                                     |                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|---------------------------------------------------------------------------|-------------|---------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <u>Nome da atividade</u>                                                  | Ano/CI      | Tipo de estudo                                                      | Objetivos                                                                                                                                                                                                             | Marcos                                                                                                                                                                                                                                                                                                                                   | Critérios de aceitação potencial                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021<br>TMC | Inquérito clínico pós-comercialização - inquérito de alta qualidade | Inquérito pós-comercialização para recolher feedback prospetivo relacionado com a utilização do FemoSeal™ Vascular Closure Device distribuído nos mercados da União Europeia.                                         | <ul style="list-style-type: none"> <li>120 casos</li> <li>8 médicos únicos com &gt; 5 anos de experiência</li> <li>Vários países na Europa</li> </ul>                                                                                                                                                                                    | <b>Avaliações de dispositivos na escala 1-5 – Afirmções de inquéritos</b> <ul style="list-style-type: none"> <li>Critérios de aceitação <ul style="list-style-type: none"> <li>As classificações 3-5 são consideradas favoráveis</li> <li>Todas as afirmações devem ter um feedback <math>\geq 80\%</math> positivo</li> </ul> </li> <li>Resultados <ul style="list-style-type: none"> <li>Nenhuma afirmação de inquérito recebida &gt; 20% de respostas desfavoráveis</li> <li>Não foram apresentadas reclamações contra o produto</li> </ul> </li> </ul> |
| 20210298 – 0,035” and 0038” Guidewire Clinical Survey Report (2021)       | 2021<br>TMC | Inquérito clínico pós-comercialização - inquérito de alta qualidade | Inquérito pós-comercialização para recolher feedback prospetivo relacionado com a utilização do fio-guia de 0,035” incluído com o Angio-Seal™ VIP Vascular Closure Device (VCD) de 6Fr e 0,038” incluído com o Angio- | <ul style="list-style-type: none"> <li>Inquéritos para fio de 0,035” <ul style="list-style-type: none"> <li>106 inquéritos</li> <li>64 médicos</li> </ul> </li> <li>Inquéritos para fio de 0,035” <ul style="list-style-type: none"> <li>109 inquéritos</li> <li>55 médicos</li> </ul> </li> <li>12 inquéritos retrospectivos</li> </ul> | <b>Avaliações de dispositivos na escala 1-5 – Afirmções de inquéritos</b> <ul style="list-style-type: none"> <li>Critérios de aceitação <ul style="list-style-type: none"> <li>As classificações 3-5 são consideradas favoráveis</li> <li>Todas as afirmações devem ter um feedback <math>\geq 80\%</math> positivo</li> </ul> </li> <li>Resultados</li> </ul>                                                                                                                                                                                             |



| Atividades de acompanhamento clínico pós-comercialização concluídas                                                                                                         |                             |                                                                                  |                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                             |                             |                                                                                  | Seal™ VIP<br>VCD de 8 Fr e<br>o FemoSeal<br>Vascular<br>Closure System<br>distribuídos nos<br>mercados da<br>União<br>Europeia.                                 |                                                                                                                                                                                                                                                                                                                                                                                          | <ul style="list-style-type: none"> <li>○ Todos os fios-guia receberam classificações aceitáveis</li> <li>○ Não foram apresentadas reclamações contra o produto</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| FemoSeal™<br>Vascular<br>Closure<br>System<br>PMCF<br>Clinical<br>Survey<br>Report:<br>Addressing<br>Gaps<br>Identified in<br>CER-FS-<br>2021 and<br>CER-FS-<br>2022 (2023) | 2023-<br>2024<br><br>TMC/TE | Inquérito<br>clínico pós-<br>comercialização<br>- inquérito de<br>alta qualidade | Recolher, de<br>forma<br>prospetiva,<br>feedback<br>relacionado<br>com a<br>utilização do<br>FemoSeal VCS<br>com fios-guia<br>distribuídos no<br>mercado da UE. | <ul style="list-style-type: none"> <li>• 126 Inquéritos <ul style="list-style-type: none"> <li>• 7 locais</li> <li>• 5 países</li> </ul> </li> <li>• 14 de novembro de 2023<br/>- 11 de junho de 2024</li> <li>• Especialidade do médico: <ul style="list-style-type: none"> <li>○ Cirurgia vascular</li> <li>○ Radiologia intervencionista</li> <li>○ Angiologia</li> </ul> </li> </ul> | <b>Avaliações de dispositivos à escala<br/>5 – Afirmações de inquéritos</b> <ul style="list-style-type: none"> <li>• Critérios de aceitação <ul style="list-style-type: none"> <li>○ As classificações 3-5 são consideradas favoráveis</li> <li>○ Todas as afirmações devem ter um feedback ≥ 80% positivo</li> <li>○ Se ocorrerem eventos adversos neste inquérito, devem ser os previstos pela gestão de risco.</li> </ul> </li> <li>• Dados demográficos de pacientes: <ul style="list-style-type: none"> <li>○ Feminino: 29,4% (37/126)</li> <li>○ Masculino: 69,8% (88/126)</li> <li>○ Sexo não divulgado: 0,8 (1/126)</li> <li>○ Idade &gt;75 anos: 31,7%</li> </ul> </li> <li>• Resultados <ul style="list-style-type: none"> <li>○ Fio-guia fornecida com o FemoSeal™ VCS: 101/126 (80,2%).</li> </ul> </li> </ul> |

| Atividades de acompanhamento clínico pós-comercialização concluídas |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|---------------------------------------------------------------------|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                     |  |  |  |  | <ul style="list-style-type: none"> <li>○ Duração do procedimento (minutos): 63,4 (36,6) (média (SD)); 57,0 (36,0-81,0) (Mediana (IQR))</li> <li>○ Todas as classificações de desempenho do FemoSeal™ VCS foram favoráveis.</li> <li>○ Todas as classificações do fio-guia fornecido pelo FemoSeal™ VCS foram favoráveis.</li> <li>○ Um (0,8%) evento adverso: os discos FemoSeal™ VCS não estavam bem alinhados provavelmente devido à utilização de um fio-guia rígido (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 polegadas) que exigia compressão manual para alcançar a hemóstase.</li> </ul> |

A Terumo Medical Corporation realizou três inquéritos de alta qualidade aos utilizadores médicos durante o atual período de comunicação (1 de setembro de 2019 a 31 de agosto de 2024).

Os inquéritos clínicos do FemoSeal™ recolheram dados clínicos proativos relativamente à segurança e desempenho do FemoSeal™ VCS durante a utilização clínica. O inquérito incluiu perguntas focadas no dispositivo global e acessórios associados, incluindo o fio-guia de 0.038" e as suas interações diretas. Os inquéritos clínicos sobre o fio-guia recolheram dados clínicos proativos relativos à segurança e desempenho durante a utilização clínica do fio-guia de 0.038" fornecido com o FemoSeal™ VCS. As perguntas do inquérito focaram-se especificamente na utilização geral do fio-guia, desde a inserção através da bainha de procedimento na vasculatura até à remoção do fio-guia.

O FemoSeal™ VCS e o fio-guia de 0.038" incluídos com o dispositivo receberam todas as classificações aceitáveis e foram apresentadas seis (6) reclamações para o dispositivo e nove (9) não reclamações para o fio-guia, com base na avaliação dos comentários recebidos dos inquéritos clínicos de alta qualidade. As reclamações foram avaliadas tanto para o FemoSeal como para o fio-guia e foram avaliadas como parte do processo de vigilância pós-comercialização da Terumo. Não foram identificados riscos e/ou níveis de risco novos.

Foi realizado um inquérito aos utilizadores médicos em 2024 no âmbito das atividades do PMCF. Os resultados do inquérito demonstraram que a classificação de desempenho e segurança do FemoSeal™ VCS foram, no geral, muito favoráveis. Também foi demonstrada a compatibilidade de outros fios-guia que não o padrão fornecido com o FemoSeal™ VCS.

#### **1.4.3.2 Acompanhamento clínico pós-comercialização em curso/planeado**

A TMC tem uma atividade de acompanhamento clínico pós-comercialização em curso/planeada. Será realizado um inquérito clínico para recolher de forma prospetiva feedback relacionado com a utilização do fio-guia com o FemoSeal VCS distribuído no mercado da UE. O inquérito será preenchido por médicos para apurar que fios-guia utilizaram durante o procedimento. O objetivo deste inquérito é resolver uma lacuna identificada como a falta de literatura e comentários de revisores externos sobre a compatibilidade do FemoSeal™ VCS com a utilização de outros fios-guia de marcas não Terumo. O feedback inclui resultados técnicos, desempenho clínico e segurança no que diz respeito ao desempenho do dispositivo com fios-guia diferentes.

#### **1.4.4 Resumo de dados da revisão sistemática da literatura**

A Terumo Medical Corporation realiza revisões sistemáticas da literatura para recolher e avaliar dados de segurança clínica e desempenho de estudos publicados sobre o FemoSeal™ VCS e/ou dispositivos similares. O objetivo do rastreio anual da literatura publicada é identificar efeitos secundários desconhecidos anteriormente, monitorizar efeitos secundários conhecidos, identificar riscos emergentes e identificar possível uso indevido sistemático ou utilização não conforme com o rótulo do FemoSeal™ VCS.

A mais recente revisão sistemática da literatura, que abrangeu o período de 1 de setembro de 2019 a 31 de agosto de 2024, identificou 29 estudos publicados que forneceram dados de segurança e desempenho clínico sobre o FemoSeal™ VCS. Vinte e três referências reportaram a utilização conforme com o rótulo do FemoSeal™ VCS e a utilização não conforme com o rótulo foi reportada em nove estudos. Em geral, a revisão da literatura de estudos específicos sobre o uso do FemoSeal™ VCS mostra uma população sob estudo que é representativa de pacientes na UE submetidos a procedimentos de cateterização vascular percutânea. Consulte a **Seção 3** para ver uma lista destas 23 publicações de utilizações conformes com o rótulo revistas por pares.

O desempenho clínico foi avaliado pelas seguintes medidas:

- O tempo até à hemóstase é melhor do que ou comparável com o Estado da Arte para a oclusão percutânea da artéria femoral comum.
- O tempo até à ambulância é melhor do que ou comparável com o Estado da Arte para a oclusão percutânea da artéria femoral comum.
- A taxa de complicações pós-operatórias é comparável ou inferior aos padrões atuais de cuidados.

Com base nestas medidas de desempenho clínico, os dados nesta revisão da literatura demonstraram que o FemoSeal™ VCS pode ser utilizado com sucesso na oclusão da punção arterial femoral (arteriotomia) em pacientes que foram submetidos a cateterização percutânea utilizando uma bainha de procedimento de 7 Fr ou mais pequena. A hemóstase completa foi alcançada na maioria dos pacientes (79,65-100%) dos casos e foi associada a um tempo médio até à hemóstase de 0,5 min, tempo médio até à alta de 3 dias. Entre 69,2 e 86,7% dos pacientes conseguiram deambular 5 h após a oclusão, com um repouso pós-operatório médio de 349 min. Foi observada falha do FemoSeal™ VCS em 3,68 a 4% dos casos e foi necessária compressão manual adicional em 0,9 a 4,4% dos procedimentos.

A segurança clínica foi avaliada por eventos adversos, incluindo, entre outros:

- Hemorragia
- Hematoma
- Pseudoaneurisma
- Queimadura
- Fístula arteriovenosa
- Infecção
- Morte

Para cada um destes eventos adversos, a taxa de ocorrência reportada para o FemoSeal™ VCS nos estudos incluídos foi inferior ou comparável às taxas reportadas historicamente para compressão manual e outros dispositivos de oclusão vascular.

Não foram identificados eventos adversos através da revisão de 10 relatórios de caso, uma vez que não foram identificados riscos novos, imprevistos, emergentes ou inaceitáveis.

A eficácia global da utilização do FemoSeal™ VCS durante a angiografia diagnóstica ou operações intervencionais depende de vários fatores, tais como: sexo, idade, anatomia do paciente, comorbidades, colocação anatômica do local de punção, experiência do cirurgião, método de colocação do VCD, cuidados pós-operatórios, etc. Além do sucesso técnico, incluindo a obtenção de hemóstase, o FemoSeal™ VCS ofereceu benefícios clínicos em relação à oclusão vascular após punção arterial femoral, tais como redução do tempo até à hemóstase, redução do tempo até à ambulação. Os resultados de desempenho para o FemoSeal™ VCS são consistentes com os esperados para este tipo de dispositivo quando utilizado conforme pretendido. Algumas das referências obtidas durante o período de investigação atual mostraram a utilização do dispositivo sujeito num local anatômico diferente da artéria femoral comum e para a oclusão de arteriotomias > 7 Fr, o que é considerado não conforme com o rótulo.

Não foram identificados efeitos secundários desconhecidos, riscos emergentes ou possível má utilização sistemática do dispositivo durante a revisão. No entanto, se o FemoSeal™ VCS for utilizado com cuidado por médicos com formação, o dispositivo médico funciona como um dispositivo clínico útil e necessário. Em geral, a terapia alvo e, por conseguinte, o FemoSeal™ VCS respondem à necessidade clínica que atualmente existe no tratamento de complicações relacionadas com o acesso vascular.

Em geral, os dados nesta revisão da literatura não identificaram qualquer problema de desempenho ou segurança no contexto clínico que fosse desconhecido previamente, ou efeitos adversos que tenham ocorrido a taxas superiores às previstas/aceitáveis. Por conseguinte, pode concluir-se desta revisão da literatura que o FemoSeal™ VCS, quando utilizado para fornecer compressão para hemóstase na arteriotomia após cateterização percutânea, continua a ter o desempenho esperado e não está associado a eventos de segurança graves.

#### **1.4.5 Resumo de dados de vigilância pós-comercialização**

Está em vigor um sistema PMS proativo e é realizada mensalmente uma revisão de todas as reclamações, em conformidade com os procedimentos internos de fabrico. Os dados de reclamação foram analisados durante o período de 1 de setembro de 2018 a 31 de agosto de 2024. Em geral, foram apresentados ao fabricante 28 relatórios de vigilância de dispositivos médicos (MDV) e 476 relatórios de reclamações de clientes. Dos 28 relatórios de MDV, 27 estavam relacionados com eventos adversos e um com mau funcionamento do dispositivo. Houve duas mortes durante o período de reporte, mas nenhuma das mortes reportadas foi considerada relacionada com o dispositivo do indivíduo. Entre as 476 reclamações apresentadas ao fabricante, as razões mais comuns para reclamar foram dificuldades de implementação (146

ocorrências, taxa de ocorrência de 0,0142%). O modo de falha de eventos de extração é o segundo mais frequente com uma taxa de 0,0126% (130 eventos).

O FemoSeal™ Vascular Closure System tem mais de 1.030.136 vendas a nível global e 827.843 no Espaço Económico Europeu. A frequência calculada das reclamações com base nas vendas globais é de 0,046%. A taxa global de reclamações de clientes é muito baixa. Não foram identificados riscos novos que não estejam incluídos nas Instruções de Utilização e na documentação de risco.

As taxas de ocorrência para os efeitos secundários indesejáveis são apresentadas na **Tabela 1.2**. Não foram identificados riscos não previstos, emergentes ou inaceitáveis entre as reclamações. Não houve aumentos significativos na frequência ou gravidade de efeitos secundários indesejáveis conhecidos.

#### 1.4.6 Resumo geral do desempenho clínico e segurança

O FemoSeal™ VCS é indicado para utilização no oclusão da punção arterial femoral comum (arteriotomia) em pacientes que tenham sido submetidos a cateterização percutânea utilizando uma bainha de procedimento de 7F (2,33 mm) ou mais pequena. Esta avaliação clínica baseia-se numa análise abrangente dos dados clínicos pré-comercialização e pós-comercialização disponíveis e da literatura relevante para a utilização prevista do FemoSeal™ VCS.

Foi realizada uma revisão alargada da literatura publicada que abrangeu o período de 1 de setembro de 2019 a 31 de agosto de 2024. O conjunto de evidências incluiu 29 estudos para o FemoSeal™ VCS. As evidências fornecidas na avaliação clínica concluem que, quando utilizado conforme indicado, o dispositivo em questão é seguro e eficaz e quaisquer riscos ou efeitos secundários indesejáveis, que possam estar associados ao dispositivo em condições normais de utilização, constituem riscos aceitáveis quando ponderados em relação aos benefícios para o paciente. Os resultados de desempenho para os dispositivos em questão são consistentes com os esperados para este tipo de dispositivo quando utilizado conforme pretendido.

Os efeitos secundários indesejáveis potenciais associados à utilização do FemoSeal™ VCS incluem os eventos adversos reportados habitualmente com meios alternativos de oclusão da arteriotomia, p. ex., hemorragia e hematoma. Globalmente, as taxas de ocorrência dos eventos adversos comunicados sobre a utilização do FemoSeal™ VCS são semelhantes às taxas reportadas com compressão manual e dispositivos de oclusão vascular semelhantes. Especificamente, para hemorragia e hematoma, as taxas reportadas para o FemoSeal™ VCS são inferiores às taxas reportadas para dispositivos de oclusão vascular semelhantes. Cada um dos eventos adversos comunicados, tanto da literatura publicada como da vigilância pós-comercialização, foi identificado anteriormente (ver **Secção 1.3**).

Os dados existentes relativos à segurança e desempenho clínico de FemoSeal™ VCS sugerem que os benefícios do paciente decorrentes da utilização deste dispositivo de oclusão vascular superam riscos possíveis quando é utilizado de acordo com as Instruções de Utilização.

Conforme indicado nas secções anteriores, os dados fornecidos para o FemoSeal™ VCS demonstram a coerência entre os dados relacionados com o dispositivo em análise (p. ex., utilização do dispositivo, resultados de segurança, desempenho clínico e benefícios clínicos), dispositivos equivalentes identificados e dados relacionados com dispositivos semelhantes enumerados no Estado da Arte.

A análise cruzada dos dados de segurança não identificou qualquer discrepância entre o seguinte:

- Dados mencionados no Estado da Arte
- Dados específicos do dispositivo em avaliação
- Dados mencionados no(s) Ficheiro(s) de gestão de risco
- Os dados mencionados na rotulagem e/ou nas IU (ou seja, são abordados os riscos residuais a serem transmitidos ao utilizador).

A segurança clínica foi demonstrada por taxas reduzidas de complicações identificadas na literatura clínica publicada revista por pares, estudos clínicos patrocinados pela empresa, revisão dos dados pós-comercialização associados sem retiradas de mercado. Não foi identificada nenhuma preocupação com o desempenho, a literatura revista continha a utilização do FemoSeal™ VCS que era consistente com a utilização prevista pelo fabricante.

### **1.5 Possíveis alternativas terapêuticas ou de diagnóstico**

Tradicionalmente, a compressão manual é utilizada para obter a hemóstase no local da arteriotomia após cateterizações vasculares. A compressão manual tem sido associada ao facto de o paciente estar imobilizado durante longos períodos de tempo (até 8 horas após um procedimento) e com desconforto substancial e internamentos hospitalares prolongados. Uma revisão sistemática recente concluiu que o tempo mediano até alcançar a hemóstase com compressão manual foi 20,8 minutos.<sup>1</sup>

As alternativas à compressão manual incluem dispositivos hemostáticos externos que aplicam compressão mecânica ao local da arteriotomia. Estes dispositivos não encurtam o tempo até à hemóstase ou o tempo até à deambulação, mas reduzem os requisitos do pessoal ao substituir a compressão manual por compressão mecânica. As taxas de eventos adversos associados à utilização de compressão mecânica são semelhantes às taxas da compressão manual.

Os dispositivos de oclusão vascular, como o FemoSeal™ VCS, foram concebidos para fechar a arteriotomia. O objetivo é reduzir o tempo até à hemóstase e permitir uma deambulação precoce. Uma revisão sistemática recente, incluindo 13 dispositivos disponíveis comercialmente, verificou que o tempo mediano até alcançar a hemóstase com um dispositivo de oclusão vascular



foi 5,4 minutos. O tempo mediano de hemóstase para os dispositivos de oclusão vascular individual variava entre 1 minuto (FemoSeal™ VCS) e 14 minutos; sendo a maioria dos dispositivos entre 4 e 10 minutos.<sup>1</sup>

Os eventos adversos reportados frequentemente associados à oclusão do local da arteriotomia, com compressões manuais, dispositivos hemostáticos externos ou dispositivos de oclusão vascular, incluem hematoma, hemorragia no local de acesso, pseudoaneurisma, fístula arteriovenosa e infecção. A mesma revisão sistemática (34 ensaios controlados aleatorizados, 14.401 pacientes) descobriu que as taxas de eventos adversos eram semelhantes entre a compressão manual e a utilização de dispositivos de oclusão vascular, com a exceção de que a hemorragia tendia a ser um pouco mais elevada com dispositivos de oclusão vascular.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Perfil de utilizador e formação sugeridos

Os utilizadores previstos do FemoSeal™ Vascular Closure System são médicos com formação que os qualifica para a realização do acesso arterial e oclusão de procedimentos endovasculares através da artéria femoral comum e que tenham participado num programa de instruções para médicos sobre o FemoSeal™ da Terumo Medical Corporation.

## 1.7 Normas harmonizadas e comuns relevantes

| Referência padrão | Ano atual de conformidade/Rev. | Descrição                                                                                                                                |
|-------------------|--------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070         | 2014/AMD1:2018                 | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070      | 2014/A1:2018                   | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance      | 20 de maio de 2021             | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052        | 2015                           | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |



| Referência padrão | Ano atual de conformidade/Rev. | Descrição                                                                                                                                                                |
|-------------------|--------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F2213        | 2017                           | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment                                             |
| ASTM F2503        | 2020                           | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                                                           |
| ASTM F2182        | 2019                           | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging                                    |
| EN ISO 13485      | 2016/A11:2021                  | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 13485         | 2016                           | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 14644-1       | 2015                           | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1    | 2015                           | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2       | 2015                           | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2    | 2015                           | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3       | 2019                           | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3    | 2019                           | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |

| Referência padrão     | Ano atual de conformidade/Rev. | Descrição                                                                                                                                     |
|-----------------------|--------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14698-1           | 2003                           | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                         |
| EN ISO 14698-1        | 2003                           | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                         |
| ISO 14698-2           | 2003/TC1:2004                  | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| EN ISO 14698-2        | 2003/TC 1:2004                 | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| USP <788>             | N/A                            | PARTICULATE MATTER IN INJECTIONS                                                                                                              |
| Farmacopeia UE 2.9.19 | N/A                            | Particulate Contamination: Sub-Visible Particles                                                                                              |
| IEC 62366-1           | 2015                           | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN 62366-1            | 2015                           | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN ISO 14971          | 2019/A11:2021                  | Medical devices — Application of risk management to Medical devices                                                                           |
| ISO 14971             | 2019                           | Medical devices — Application of risk management to Medical devices                                                                           |
| ASTM F1980            | 2016                           | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                                           |
| EN ISO 10993-1        | 2020                           | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                    |
| ISO 10993-1           | 2018                           | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                    |
| EN ISO 10993-2        | 2006                           | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                                                |

| Referência padrão | Ano atual de conformidade/Rev. | Descrição                                                                                                            |
|-------------------|--------------------------------|----------------------------------------------------------------------------------------------------------------------|
| ISO 10993-2       | 2006                           | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3    | 2014                           | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3       | 2014                           | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4    | 2017                           | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4       | 2017                           | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| EN ISO 10993-5    | 2009                           | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| ISO 10993-5       | 2009                           | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| EN ISO 10993-6    | 2016                           | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |
| ISO 10993-6       | 2016                           | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |
| EN ISO 10993-10   | 2023                           | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                       |
| ISO 10993-10      | 2021                           | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                       |
| EN ISO 10993-11   | 2018                           | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                      |
| ISO 10993-11      | 2017                           | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                      |
| EN ISO 10993-12   | 2021                           | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                       |

| Referência padrão | Ano atual de conformidade/Rev. | Descrição                                                                                                                                  |
|-------------------|--------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-12      | 2021                           | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| EN ISO 10993-17   | 2009                           | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17      | 2002                           | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18      | 2020/A1:2022                   | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |
| EN ISO 10993-18   | 2020/A1:2022                   | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |
| EN ISO 10993-23   | 2021                           | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |
| ISO 10993-23      | 2021                           | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |
| ASTM F2382        | 2018                           | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)          |
| ASTM F756         | 2017                           | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                      |
| USP <85>          | N/A                            | [Bacterial Endotoxins Test. (Sterility)]                                                                                                   |
| USP <161>         | N/A                            | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                     |

| Referência padrão | Ano atual de conformidade/Rev. | Descrição                                                                                                                                                                    |
|-------------------|--------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ANSI/AAMI ST72    | 2019                           | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135      | 2014/A1:2019                   | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135         | 2014/A1:2018                   | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7    | 2008/A1:2022                   | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |
| ISO 10993-7       | 2008/A1:2019                   | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                                            |
| EN 556-1          | 2024                           | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices              |
| EN ISO 11737-1    | 2018/A1:2021                   | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                                        |
| ISO 11737-1       | 2018/A1:2021                   | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                                        |
| EN ISO 11138-1    | 2017                           | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                                 |
| ISO 11138-1       | 2017                           | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                                 |
| EN ISO 11138-2    | 2017                           | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                                     |

| Referência padrão | Ano atual de conformidade/Rev. | Descrição                                                                                                                                |
|-------------------|--------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11138-2       | 2017                           | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| EN ISO 15223-1    | 2016                           | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| ISO 15223-1       | 2016                           | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| EN 1041           | 2008/A1:2013                   | Information supplied by the manufacturer of medical devices                                                                              |
| EN ISO 11607-1    | 2020/A1:2023                   | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| ISO 11607-1       | 2019/A1:2023                   | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| EN ISO 11607-2    | 2020/A1:2023                   | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes       |
| ISO 11607-2       | 2019/A1:2023                   | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes       |
| ASTM D4169        | 2016                           | Standard Practice for Performance Testing of Shipping Containers and Systems                                                             |
| ASTM F1886/F1886M | 2016                           | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                      |
| ASTM F2825        | 2018                           | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                 |

| Referência padrão | Ano atual de conformidade/Rev. | Descrição                                                                                                                                                                          |
|-------------------|--------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F2096        | 2011 (R 2019)                  | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                                       |
| ASTM F88/F88M     | 2015                           | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                               |
| MDCG 2021-24      | 2021                           | Guidance on classification of medical devices                                                                                                                                      |
| MDCG 2020-3       | 2020                           | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD         |
| MDCG 2020-8       | 2020                           | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                                     |
| MDCG 2020-7       | 2020                           | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                                  |
| MDCG 2020-6       | 2020                           | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                               |
| MDCG 2019-9 v1    | 2022                           | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                           |
| MDCG 2019-8 v2    | 2020                           | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices |
| MDCG 2020-15      | 2020                           | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                           |
| MDCG 2021-11      | 2021                           | Guidance on Implant Card – ‘Device types’                                                                                                                                          |
| MDCG 2021-19      | 2021                           | Guidance note integration of the UDI within an organisation’s quality management system                                                                                            |

| Referência padrão   | Ano atual de conformidade/Rev. | Descrição                                                                                                                                                                                                                                                     |
|---------------------|--------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2018-1 v4      | 2021                           | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2         | 2019                           | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1         | 2019                           | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7         | 2018                           | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6         | 2018                           | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |
| MDCG 2018-4         | 2018                           | MDCG 2018-4 Annex: UDI database Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                                                                                                  |
| MDCG 2018-3 v1      | 2020                           | Guidance on UDI for systems and procedure packs                                                                                                                                                                                                               |
| MDCG 2021-25        | 2021                           | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC                                                                 |
| Meddev 2.12-2 Rev 2 | 2012                           | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                                                                                        |



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### 3.0 HISTÓRICO DE REVISÕES

| Número de revisão do SSCP | Data de emissão       | Descrição da alteração                                                     | Revisão validada pelo organismo notificado                                                                                                                                                                                                                                                                                                        |
|---------------------------|-----------------------|----------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022              | 20 de janeiro de 2023 | Emissão inicial, após certificação CE do RDM                               | <p><input checked="" type="checkbox"/> Sim</p> <p>Idioma da validação: English</p> <p><input type="checkbox"/> Não (aplicável apenas para dispositivos implantáveis de classe IIa ou alguns IIb (MDR, Artigo 52 (4), 2.º parágrafo) para os quais o SSCP ainda não foi validado pelo ON)</p> <p><input type="checkbox"/> Outro (especifique):</p> |
| SSCP-FS-2023 – Revisão 1  | 15 de março de 2024   | Atualizado para o período de 1 de janeiro de 2019 a 31 de dezembro de 2023 | <p><input checked="" type="checkbox"/> Sim</p> <p>Idioma da validação: English</p> <p><input type="checkbox"/> Não (aplicável só para dispositivos implantáveis de classe IIa ou alguns IIb (RDM, Artigo 52.º (4), 2.º parágrafo) para os quais o SSCP ainda não foi validado pelo ON)</p> <p><input type="checkbox"/> Outro (especifique):</p>   |
| SSCP-FS-2024 Revisão 1    |                       | Atualizado para o período de 1 de setembro de 2019 a 31 de agosto de 2024. | <p><input type="checkbox"/> Sim</p> <p>Idioma da validação: English</p> <p><input type="checkbox"/> Não (aplicável só para dispositivos implantáveis de classe IIa ou alguns IIb (RDM, Artigo 52.º (4), 2.º parágrafo) para os quais o SSCP ainda não foi validado pelo ON)</p> <p><input type="checkbox"/> Outro (especifique):</p>              |

|                           |               |                                                            |                                                                                                                                                                                                                                                                                                                                                                                     |
|---------------------------|---------------|------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>Revisão 2 | June 20, 2025 | Revisto com base em<br>consultas do NSAI para<br>validação | <div><input checked="" type="checkbox"/> Sim</div> <div>Idioma da validação: English</div> <div><input type="checkbox"/> Não (aplicável só para<br/>dispositivos implantáveis de<br/>classe IIa ou alguns IIb (RDM,<br/>Artigo 52.º (4), 2.º parágrafo)<br/>para os quais o SSCP ainda não<br/>foi validado pelo ON)</div> <div><input type="checkbox"/> Outro (especifique):</div> |
|---------------------------|---------------|------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

## Rezumatul caracteristicilor de siguranță și performanță clinică

### FemoSeal™ Vascular Closure System

|                                                                             |                                                                                             |
|-----------------------------------------------------------------------------|---------------------------------------------------------------------------------------------|
| <b>Producător</b>                                                           | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 S.U.A.      |
| <b>Număr unic de înregistrare (SRN)<br/>al producătorului</b>               | US-MF-000019594                                                                             |
| <b>Reprezentant al conducerii/PRRC</b>                                      | Kimberly Feitl<br>Vicepreședinte, Calitate                                                  |
| <b>UDI-DI de bază</b>                                                       | 38970FS79                                                                                   |
| <b>Număr EMDN</b>                                                           | C900199 – Sisteme hemostatice – Altele                                                      |
| <b>Clasa dispozitivului</b>                                                 | Clasa III                                                                                   |
| <b>Anul în care dispozitivul a primit<br/>pentru prima dată marcajul CE</b> | 2005                                                                                        |
| <b>Reprezentant în UE</b>                                                   | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgia<br>SRN: BE-AR-000001433 |
| <b>Organism notificat</b>                                                   | NSAI<br>CE 0050                                                                             |

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Acest rezumat al caracteristicilor de siguranță și performanță clinică (SSCP) are scopul de a oferi acces public la un rezumat actualizat al principalelor aspecte de siguranță și performanță clinică ale FemoSeal™ Vascular Closure System (VCS).

Un rezumat al caracteristicilor de siguranță și performanță clinică, conceput pentru utilizatori/profesioniști în domeniul sănătății, este prezentat mai jos în **Secțiunea 1.0**.

## **1.0 REZUMAT PENTRU UTILIZATORI/PROFESIONIȘTI ÎN DOMENIUL SĂNĂTĂȚII**

SSCP nu are scopul de a înlocui Instrucțiunile de utilizare ca document principal care asigură utilizarea dispozitivului în condiții de siguranță și nici nu are scopul de a oferi sugestii de diagnosticare sau terapeutice utilizatorilor sau pacienților propuși. SSCP nu are scopul de a înlocui informațiile obligatorii de pe cardurile de implant sau din alte documente obligatorii.

### **1.1 Utilizarea preconizată a produsului**

#### **1.1.1 Utilizare preconizată**

FemoSeal™ Vascular Closure System este un dispozitiv medical destinat închiderii unei puncții arteriale după cateterizarea percutanată prin artera femurală comună.

#### **1.1.2 Instrucțiuni de utilizare**

FemoSeal™ Vascular Closure System este indicat pentru utilizare la închiderea puncției arteriale femurale comune (arteriotomie) la pacienții care au fost supuși cateterizării percutanate utilizând o teacă procedurală de 7 F (2,33 mm) sau mai mică.

#### **1.1.3 Contraindicații și/sau limitări**

FemoSeal™ Vascular Closure System este contraindicat la pacienții cu arteriotomii la care s-au utilizat teci sau dispozitive mai mari de 7 F (2,33 mm).

#### **1.1.4 Populații de pacienți țintă**

Siguranța și eficacitatea FemoSeal™ Vascular Closure System au fost stabilite la pacienții cu vârsta de cel puțin 18 ani care au fost supuși cateterizării percutanate utilizând o teacă procedurală de 7 F (2,33 mm) sau mai mică.

#### **1.1.5 Populații speciale de pacienți**

Siguranța și eficacitatea FemoSeal™ Vascular Closure System nu au fost stabilite pentru următoarele populații de pacienți:

- Pacienți cu boală autoimună preexistentă.
- Pacienți supuși unei trombolize terapeutice.
- Pacienți cu boală vasculară periferică semnificativă din punct de vedere clinic.
- Pacienți cu hipertensiune arterială necontrolată ( $> 220$  mmHg sistolică sau  $> 110$  mmHg diastolică).
- Pacienți cu tulburare hemoragică, inclusiv trombocitopenie (număr de trombocite  $< 100.000$ ) sau anemie (Hgb  $< 10$  mg/dl).

- Pacienți cu un lumen interior al arterei femurale comune mai mic de 5 mm.
- Pacienți cu insuficiență renală și/sau hepatică.
- Pacienți cu altă comorbiditate relevantă.
- Populație cu origini rasiale și/sau etnice specifice.
- Pacienți cu infarct miocardic înainte cu maximum 72 de ore.
- Pacienți cu grefă vasculară sau stent la locul puncției.
- Paciente gravide sau care alăptează.
- Pacienți cu vârsta sub 18 ani.

### 1.1.6 Utilizatorii preconizați

Utilizatorii propuși ai FemoSeal™ Vascular Closure System sunt medici cu instruire care îi califică pentru efectuarea abordului arterial și a închiderii pentru procedurile endovasculare prin artera femurală comună și care au participat la programul de instruire pentru medici al Terumo Medical Corporation FemoSeal™.

## 1.2 Descrierea dispozitivului

### 1.2.1 Descrierea dispozitivului

FemoSeal™ Vascular Closure System, fabricat de Terumo Medical Corporation (TMC), este un dispozitiv de închidere vasculară resorbabil, conceput pentru a realiza hemostaza arterială femurală după cateterizarea percutanată prin artera femurală comună.

Elementele de închidere FemoSeal™ constau din două discuri polimerice resorbabile, garnitura interioară și discul de blocare exterior, care sunt menținute împreună cu un filament multiplu resorbabil, etanșând astfel mecanic arteriotomia (consultați **Figura 1.1** și **Figura 1.2**). După ce a fost aplicat prin teaca cu carcasă conică, discul de blocare exterior este fixat pe axul filamentului multiplu, având ca rezultat închiderea mecanică a locului puncției între discul interior și discul de blocare exterior. Garnitura interioară și discul de blocare exterior sunt menținute prin frecare pe axul filamentului multiplu. Hemostaza se realizează prin mijloace mecanice. Elementele de închidere sunt degradate prin hidroliză.

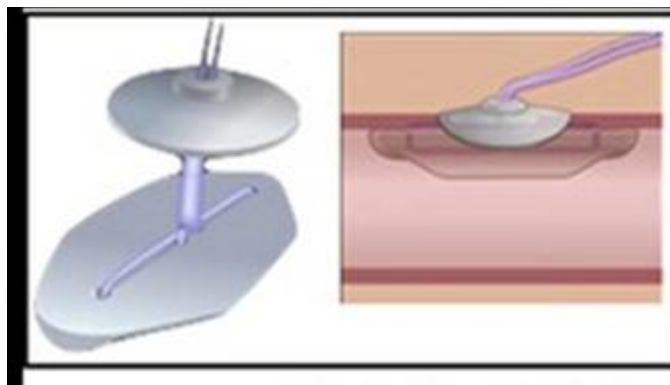
Componentele de închidere implantabile, garnitura interioară și discul de blocare exterior, se degradează în optsprezece (18) luni, în timp ce filamentul multiplu este estimat a se degrada și a fi resorbit prin hidroliză de țesutul înconjurător după doi (2) până la trei (3) ani. Capacitatea componentelor de închidere implantabile de a menține compresia pe arteriotomie a fost testată la o perioadă de până la opt (8) ore. Producții de degradare sunt metabolizați și excretați în urină sau

expirați prin plămâni sub formă de dioxid de carbon. Nu au fost observate efecte de acumulare în studiile efectuate pe animale. Componentele suplimentare ale FemoSeal™ care vor intra în contact cu țesutul viu sau cu sângele în timpul procedurii sunt teaca cu carcasă conică, dilatatorul, tubul de tasare, dispozitivul de împingere și firul de ghidaj.

**Figura 1.1 Garnitură interioară și, respectiv, disc de blocare exterior**

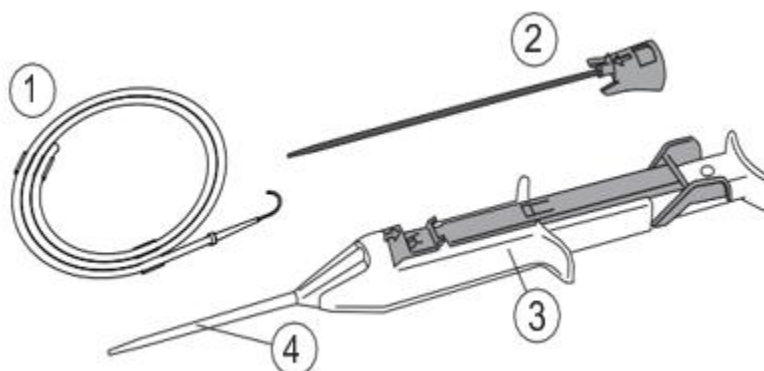


**Figura 1.2 Garnitură interioară și disc de blocare exterior introduse**



Unitatea FemoSeal™ este ambalată împreună cu un dilatator și un fir de ghidaj cu DE de 0,038" (0,97 mm) și lungime de 27,5" (70 cm) și un dispozitiv de îndreptare în formă de J; consultați **Figura 1.3** de mai jos. Firul de ghidaj este inclus într-un tub din polietilenă. Toate piesele sunt ambalate într-o tavă de hârtie rigidă. Ambalajul include și cardul de implant al pacientului. FemoSeal™ Vascular Closure System nu necesită accesorii suplimentare pentru ca dispozitivul să funcționeze conform scopului propus, iar dispozitivul este destinat exclusiv utilizării cu dilatatorul și firul de ghidaj incluse în ambalajul produsului.

**Figura 1.3 Unitatea FemoSeal™ VCS cu fir de ghidaj și dilatator**



## 1.2.2 Materii prime și componente

Tabelul 1.1 de mai jos enumeră componentele FemoSeal™ VCS.

**Tabelul 1.1 Materii prime și componentele FemoSeal™**

| Cod | Descriere                                                                                       |                                                                | Materiale                                                                                                                                                                               |
|-----|-------------------------------------------------------------------------------------------------|----------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1   | Fir de ghidaj de 0,038" (0,97 mm) cu dispozitiv de îndreptare a firului de ghidaj în formă de J |                                                                | Fir de ghidaj: Oțel inoxidabil 304<br><br>Dispozitiv de îndreptare în formă de J: polipropilenă, pigment violet<br><br>Clemă: polietilenă<br><br>Tubulatură: polietilenă                |
| 2   | Dilatator FemoSeal                                                                              |                                                                | Ambou: tetrahidrofuran, pigment albastru, polibutilen tereftalat (PBT)<br><br>Tub: polietilenă de înaltă densitate (HDPE), pigment negru<br><br>Lubrifiant: Silicon Dow Corning 360     |
| 3/4 | Unitate FemoSeal                                                                                | RD7 turnat – garnitură interioară și disc de blocare exterior* | Copolimer între glicolidă, trimetilen-carbonat, ε-caprolactonă și TMP: trimetilolpropan (inițiator)                                                                                     |
|     |                                                                                                 | Filament multiplu*                                             | Copolimer segmentat între L,L-Lactidă, trimetilen-carbonat, ε-caprolactonă și 1,3 propandiol (inițiator)<br><br>Învelișul este un copolimer între glicolidă, ε-caprolactonă și L-lizină |
|     |                                                                                                 | Tub de manipulare                                              | Polipropilenă                                                                                                                                                                           |
|     |                                                                                                 | Dispozitiv de împingere                                        | Oțel inoxidabil 304V                                                                                                                                                                    |
|     |                                                                                                 | Glisor                                                         | Polibutilen tereftalat (PBT)                                                                                                                                                            |

|  |  |                         |                                                           |
|--|--|-------------------------|-----------------------------------------------------------|
|  |  | Carcasă                 | Polibutilen tereftalat (PBT)                              |
|  |  | Buton                   | Polibutilen tereftalat (PBT)                              |
|  |  | Capac buton             | Polioximetilenă (POM)/copolimer de poliacetal             |
|  |  | Manșon                  | Polibutilen tereftalat (PBT)                              |
|  |  | Distanțier              | Polibutilen tereftalat (PBT)                              |
|  |  | Con                     | Polipropilenă                                             |
|  |  | Capac carcasă           | Polibutilen tereftalat (PBT)                              |
|  |  | Mecanism de siguranță   | Polibutilen tereftalat (PBT), pigment albastru            |
|  |  | Capac manșon            | Polibutilen tereftalat (PBT)                              |
|  |  | Garnitură tub           | Silicon duritatea Shore A 70                              |
|  |  | Garnitură carcasă       | Silicon duritatea Shore A 50                              |
|  |  | Arc                     | Oțel inoxidabil 302                                       |
|  |  | Teacă cu carcasă conică | Polipropilenă<br>Silicon duritatea Dow Corning 360, hexan |

\* Porțiune implantabilă a dispozitivului; componentele implantabile sunt sigure în mediul IRM

FemoSeal™ VCS este sterilizat cu oxid de etilenă (EO) și este un dispozitiv medical de unică folosință. Dispozitivul FemoSeal™ VCS este conceput astfel încât să nu poată fi reutilizat.

### **Mod de acțiune**

FemoSeal™ VCS susține hemostaza mecanică prin aplicarea de elemente de închidere implantabile pe interiorul și pe exteriorul arterei femurale comune. Mecanismul care împiedică sângerarea este furnizat de garnitura interioară care sigilează locul puncției și discul de blocare exterior care menține garnitura interioară în poziție.

### **1.2.3 Beneficiu clinic**

FemoSeal™ VCS oferă următoarele beneficii clinice pentru închiderea vasculară după efectuarea puncției arterei femurale comune:

- Reducerea timpului până la hemostază<sup>1</sup>
- Reducerea timpului până la mobilizarea postoperatorie<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

#### 1.2.4 Generație/Generații sau variante anterioare

- Prima versiune a FemoSeal™ VCS (#11200) a fost comercializată pe piața europeană în cursul anului 2005 și o parte a anului 2006.
- FemoSeal™ VCS (#11202) actual, cu un sistem de introducere îmbunătățit, se află pe piață începând cu 28 martie 2006.

#### 1.2.5 Accesorii destinate utilizării în asociere cu dispozitivul

Unitatea FemoSeal™ este ambalată împreună cu un dilatator, un fir de ghidaj cu DE de 0,038" (0,97 mm) și lungimea de 27,5" (70 cm) și un dispozitiv de îndreptare în formă de J. Firul de ghidaj este un accesoriu al unității FemoSeal™. Dispozitivul de îndreptare în formă de J este o componentă a firului de ghidaj, în timp ce dilatatorul este o componentă a unității FemoSeal™. Firul de ghidaj este singurul accesoriu luat în considerare. Firul de ghidaj este inclus într-un tub din polietilenă. Toate piesele sunt ambalate într-o tavă de hârtie rigidă. Ambalajul include și cardul de implant al pacientului. FemoSeal™ Vascular Closure System nu necesită accesorii suplimentare pentru ca dispozitivul să funcționeze conform scopului propus, iar dispozitivul este destinat exclusiv utilizării cu dilatatorul și firul de ghidaj incluse în ambalajul produsului.

#### 1.2.6 Alte dispozitive și produse destinate utilizării în asociere cu dispozitivul

FemoSeal™ VCS nu necesită dispozitive suplimentare pentru a funcționa conform scopului propus.

### 1.3 Riscuri și avertismente

#### 1.3.1 Riscuri reziduale și efecte nedorite

Evenimentele adverse, vătămrile și complicațiile cunoscute sau anticipate asociate cu utilizarea FemoSeal™ VCS ca urmare a riscurilor reziduale sunt enumerate în **Tabelul 1.2**. Frecvența evenimentelor se bazează pe o analiză a documentației de risc și se calculează pe baza datelor de supraveghere ulterioare introducerii pe piață, de la 1 septembrie 2019 până pe 31 august 2024. Nu există riscuri reziduale necunoscute pentru FemoSeal™ VCS și toate riscurile aplicabile au fost abordate prin Instrucțiunile de utilizare și procesul de gestionare a riscurilor.

**Tabelul 1.2. Evenimente adverse/complicații asociate cu FemoSeal**

| Vătămare                                              | Frecvență (%) | Factori de diminuare                                                                                                                                                                                                          |
|-------------------------------------------------------|---------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Reacție alergică                                      | 0,0000        | Acțiunile și planurile de reducere cât mai mult posibil a riscurilor au fost abordate cu ajutorul funcțiilor de proiectare a produselor, instrucțiunilor de fabricație, al etichetării produselor și al instruirii medicului. |
| Anevrism                                              | 0,0000        |                                                                                                                                                                                                                               |
| Fistulă AV                                            | 0,0001        |                                                                                                                                                                                                                               |
| Pierdere de sânge/sângerare                           | 0,0280        |                                                                                                                                                                                                                               |
| Deces                                                 | 0,0002        |                                                                                                                                                                                                                               |
| Echimoză                                              | 0,0000        |                                                                                                                                                                                                                               |
| Embolie                                               | 0,0000        |                                                                                                                                                                                                                               |
| Reacție la corp străin                                | 0,0000        |                                                                                                                                                                                                                               |
| Hematom                                               | 0,0027        |                                                                                                                                                                                                                               |
| Hemoragie                                             | 0,0001        |                                                                                                                                                                                                                               |
| Infecție                                              | 0,0002        |                                                                                                                                                                                                                               |
| Reacție inflamatorie                                  | 0,0000        |                                                                                                                                                                                                                               |
| Amorțeală                                             | 0,0000        |                                                                                                                                                                                                                               |
| Durere                                                | 0,0000        |                                                                                                                                                                                                                               |
| Disconfortul pacientului                              | 0,0004        |                                                                                                                                                                                                                               |
| Întârzierea procedurii                                | 0,0065        |                                                                                                                                                                                                                               |
| Pseudoanevrism                                        | 0,0004        |                                                                                                                                                                                                                               |
| Sângerare retroperitoneală                            | 0,0002        |                                                                                                                                                                                                                               |
| Septicemie                                            | 0,0000        |                                                                                                                                                                                                                               |
| Tromboembolie                                         | 0,0000        |                                                                                                                                                                                                                               |
| Tromboză                                              | 0,0001        |                                                                                                                                                                                                                               |
| Ocluzia vasului sanguin/ischemia membrelor inferioare | 0,0002        |                                                                                                                                                                                                                               |
| Perforarea vasului                                    | 0,0000        |                                                                                                                                                                                                                               |
| Disecție/lacerație a țesutului vascular               | 0,0003        |                                                                                                                                                                                                                               |



### 1.3.2 Avertismente și precauții

#### Avertismente

1. A nu se utiliza dacă ambalajul a fost deteriorat sau dacă orice barieră sterilă nu este intactă.
2. A nu se utiliza după data de expirare – este posibil ca unele componente biodegradabile să nu mai prezinte performanța corespunzătoare.
3. A nu se utiliza dacă ambalajul pare deteriorat sau prezintă orice fel de defect.
4. Utilizarea FemoSeal™ Vascular Closure System în situațiile în care se poate să fi avut loc contaminarea bacteriană a tecii procedurale sau a țesutului înconjurător poate provoca infecții.
5. Dacă se suspectează că peretele arterial posterior a fost perforat sau s-a efectuat mai mult de o puncție arterială, nu vă bazați exclusiv pe FemoSeal™ Vascular Closure System pentru a realiza hemostaza arterială. Utilizați compresie suplimentară, manuală sau mecanică.
6. Dacă locul puncției se află în bifurcația arterei femurale sau distal față de aceasta, FemoSeal™ Vascular Closure System nu trebuie utilizat din cauza riscului ca garnitura interioară să fie poziționată incorect. Acest eveniment poate duce la complicații hemoragice și/sau la perturbarea fluxului sanguin normal.
7. Dacă există sângerări arteriale persistente la locul inciziei, nu tăiați filamentul multiplu decât după ce se realizează hemostaza. Dacă nu se realizează hemostaza, fixați filamentul multiplu cu un pansament steril și aplicați o compresie suplimentară până la realizarea hemostazei. În cazul unei hemoragii arteriale persistente pot surveni complicații hemoragice semnificative, care pot duce la vătămarea sau decesul pacientului.
8. Nu utilizați FemoSeal™ Vascular Closure System dacă locul puncției este proximal față de ligamentul inghinal, deoarece acest lucru poate avea ca rezultat un hematom retroperitoneal.
9. Pacienții care prezintă un risc crescut de sângerare pot suferi o pierdere mai mare de sânge, necesitând o transfuzie.
10. Dacă discul interior se desprinde, poate provoca un eveniment trombotic și/sau embolic.

#### Precauții

1. Procedura de introducere a FemoSeal™ Vascular Closure System trebuie efectuată de medici cu instruire adecvată în utilizarea dispozitivului.
2. Efectuați o angiogramă femurală limitată sau o puncție femurală ghidată ecografic înainte de introducerea FemoSeal™ Vascular Closure System.

3. Întrerupeți procedura dacă:
  - Diametrul lumenului arterei femurale comune < 5 mm.
  - Este prezentă stenoza și/sau depuneri semnificative în apropierea locului de puncție arterială femurală comună.
  - Puncția arterială este la bifurcația arterei femurale sau distal față de aceasta.
  - Sunt prezente ramuri anormale sau anomalii ale vaselor sanguine în apropierea locului de puncție al arterei femurale comune.
4. Dacă este prezent orice hematom, trebuie acordată o atenție suplimentară la introducerea corectă a tecii cu carcasă conică în arteră.
5. Utilizați o tehnică de puncție pe un singur perete. Nu efectuați puncția în peretele posterior al arterei.
6. Respectați întotdeauna tehnica sterilă atunci când utilizați FemoSeal™ Vascular Closure System.
7. FemoSeal™ Vascular Closure System este numai pentru unică utilizare și nu trebuie resterilizat sau reutilizat în niciun fel. Unitatea FemoSeal™ este concepută astfel încât să nu poată fi reutilizată.
8. Dacă introducerea garniturii interioare întâmpină o rezistență neașteptată, întrerupeți procedura.
9. Pentru o introducere corectă a garniturii interioare, re poziționați degetul mare astfel încât butonul să poată reveni liber.
10. Asigurați-vă că vârful tecii cu carcasă conică a unității FemoSeal™ se află sub suprafața pielii înainte de a introduce discul de blocare exterior. Discul de blocare exterior poate fi aplicat din greșeală deasupra nivelului pielii la pacienții cu o distanță scurtă între artera femurală și suprafața pielii.
11. Pentru o introducere corectă, poate fi necesară o incizie cutanată înainte de introducere.
12. Dacă garnitura interioară se află în interiorul arterei, dar nu este posibilă apăsarea completă a butonului și introducerea discului de blocare exterior, poate fi necesară intervenția chirurgicală pentru îndepărtarea elementelor de închidere FemoSeal™.
13. Dacă este necesară repetarea puncției aceleiași artere femurale în termen de 18 luni, noua puncție trebuie efectuată la cel puțin un centimetru proximal față de locul de abord anterior al FemoSeal™ Vascular Closure System.
14. Instruiți pacientul să respecte instrucțiunile medicului cu privire la inspectarea locului de închidere.
15. Instruiți pacientul să aibă asupra sa cardul cu informații pentru pacient în următoarele 18 luni

### Precauții la momentul externării

Înainte de a lua în considerare externarea, evaluați pacientul cu privire la următoarele probleme clinice:

1. Sângerare și/sau hematoame la locul de închidere.
2. Durere în timpul mersului.
3. Semne de infecție la locul de închidere.

### 1.3.3 Acțiuni corective în materie de siguranță pe teren

A existat o acțiune corectivă în materie de siguranță pe teren care a implicat FemoSeal™ VCS în perioada cuprinsă între 1 septembrie 2019 și 31 august 2024.

În 2022, Terumo a rechemat voluntar FemoSeal™ VCS din cauza reclamațiilor care invocau erorile din procesul de testare și testarea la lansarea lotului de produse FemoSeal fabricat de Elkton pentru măsurarea forței de tasare și a forței de retragere. În total au fost rechemate 950 de unități din Coreea de Sud.

## 1.4 Evaluare clinică și monitorizare clinică ulterioară introducerii pe piață

**Tabelul 1.3** include o listă a studiilor pivot incluse pentru introducerea pe piață a FemoSeal™ VCS, precum și a studiilor ulterioare introducerii pe piață și activități de monitorizare clinică ulterioare introducerii pe piață. Versiunea dispozitivului utilizat în studiu este inclusă în tabelul de mai jos. Prima versiune a FemoSeal™ VCS (#11200) a fost comercializată până în 2006, în timp ce următoarea versiune (#C11202) a fost lansată pe piață în 2006 și se află în prezent pe piață.

**Tabelul 1.3 Rezumatul studiilor pivot**

| Testarea funcțională pe animale anterior introducerii pe piață                                                                                                                                                                                                          | Versiune dispozitiv |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200               |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200               |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200               |
| Primul studiu clinic pe oameni                                                                                                                                                                                                                                          |                     |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200               |

| Studii clinice ulterioare introducerii pe piață, finalizate                                                                     |                                 |
|---------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                      | C11202<br>(dispozitivul actual) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                               | C11202<br>(dispozitivul actual) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | C11202<br>(dispozitivul actual) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)          | C11202<br>(dispozitivul actual) |
| Studii clinice ulterioare introducerii pe piață, planificate/în curs                                                            |                                 |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                      | C11202<br>(dispozitivul actual) |
| Activități de monitorizare clinică ulterioară introducerii pe piață                                                             |                                 |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(dispozitivul actual) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(dispozitivul actual) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(dispozitivul actual) |

#### 1.4.1 Rezumatul datelor provenite anterioare introducerii pe piață (din testările efectuate pe animale și investigațiile clinice)

**Tabelul 1.4** de mai jos descrie toate studiile anterioare introducerii pe piață, atât din testările efectuate pe animale, cât și din investigațiile clinice.

**Tabelul 1.4 Rezumatele studiilor anterioare introducerii pe piață**

| Testarea funcțională pe animale anterior introducerii pe piață                                 |                                   |                                                 |                                                                                                         |                                                      |                                                                                                                                   |
|------------------------------------------------------------------------------------------------|-----------------------------------|-------------------------------------------------|---------------------------------------------------------------------------------------------------------|------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|
| Denumirea studiului                                                                            | Anul/Investigator<br>coordonator  | Tipul studiului                                 | Obiective                                                                                               | Repere                                               | Criterii pentru posibila<br>acceptare                                                                                             |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the | 2000<br>Radi Medical<br>System AB | Studiu pe animale;<br>investigație exploratorie | Scopul studiului a fost evaluarea biocompatibilității și biofuncționalității unui implant biodegradabil | N = 3 oi femele adulte, 1 animal la fiecare perioadă | Permeabilitatea arterei<br>• Evaluarea fluxului sanguin după introducere – reducerea fluxului sanguin cu 2/3, asociată cu spasmul |

|                                                                                                                                                                          |                               |  |                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
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| Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | Efectuat de Biomatech, Franța |  | conceput pentru realizarea hemostazei în sistemul vascular. Raportul se referă la animalele de rezervă din studiul cu numărul 862 (document # 1051-01) | <p>Monitorizare pentru analiza histopatologică, clasificarea macroscopică și analiza ultrastructurală</p> <ul style="list-style-type: none"> <li>• 12 luni</li> <li>• 15 luni</li> <li>• 18 luni</li> </ul> <p>Monitorizare ecografică Doppler color – 30 de zile la locurile de abord în artera carotidă și femurală</p> | <p>vascular temporar al arterei, care a fost atribuit procedurii, ambele au survenit la artera carotidă comună stângă</p> <ul style="list-style-type: none"> <li>• Evaluare ecografică Doppler color (4 săptămâni) – 3/3 (100%) fără reducere importantă a fluxului sanguin la 30 de zile după implantare</li> </ul> <p>Observații macroscopice</p> <ul style="list-style-type: none"> <li>• 12 luni – permeabilitate confirmată macroscopic prin absența ocuziei vizibile anatomic; fără leziuni de intoleranță locală macroscopică (hemoragie, necroză sau neovascularizare); încapsularea discului interior părea pronunțată</li> <li>• 15 luni – observarea macroscopică nu a evidențiat semne de inflamare; nu au fost identificate reziduuri de disc interior sau exterior; țesutul de încapsulare situat în zona discului exterior a apărut ca la observarea de 12 luni</li> <li>• 18 luni – observarea macroscopică nu a evidențiat niciun semn de intoleranță locală, discul exterior vizibil (3/3 cazuri), resorbția completă a discului interior; 1/3 (artera carotidă comună stângă) – depresia peretelui arterial observată la locul implantului (ar putea fi asociată cu introducerea dispozitivului)</li> </ul> <p>Concluzii</p> <ul style="list-style-type: none"> <li>• La nivel macroscopic, după 12, 15 și 18 luni de la implantare nu au fost detectate semne necrotice, degenerative sau trombotice.</li> <li>• Procesul de degradare a discului interior și exterior a părut a progresa între 12 și 18 luni și a părut complet la 18 luni, cu un țesut</li> </ul> |
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|                                                                                                                                                                                                                                                                                |                                                                         |                                                     |                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                 | <p>albicios acoperind zona implantată.</p> <ul style="list-style-type: none"> <li>Histologic, după 18 luni, materialul polimeric nu a mai fost vizibil, dar a fost prezent un țesut fibros endoluminal. Nu au fost observate leziuni necrotice, degenerative sau trombotice.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002 Radi Medical System AB</p> <p>Efectuat de Biomatech, Franța</p> | <p>Studiu pe animale; investigație exploratorie</p> | <p>Scopul studiului a fost evaluarea biocompatibilității unui implant biodegradabil conceput pentru realizarea hemostazei în sistemul vascular.</p> | <p>Monitorizare (după implantare)</p> <ul style="list-style-type: none"> <li>12 săptămâni</li> <li>24 de săptămâni</li> <li>36 de săptămâni</li> </ul> <p>N = 12 oi, 3 animale la fiecare perioadă, 3 animale de rezervă sacrificate la 12, 15 și 18 luni</p> <p>Locuri de implantare – artera femurală dreapta și stânga, artera carotidă comună dreapta și stânga</p> <p>Analiză ecografică Doppler color</p> | <p><u>Permeabilitatea arterei carotide și femurale după 4 săptămâni</u></p> <ul style="list-style-type: none"> <li>Reducere importantă a fluxului sanguin 0/12 (0%)</li> </ul> <p><u>Nicio reducere importantă a fluxului sanguin</u></p> <ul style="list-style-type: none"> <li>Afectare severă a fluxului sanguin asociată introducerii dispozitivului 0/12 (0%)</li> <li>Reducerea fluxului sanguin în carotida comună stângă 2/12 (16,6%) din cauza spasmului venos temporar al arterei (atribut intervenției chirurgicale, nu dispozitivului)</li> </ul> <p><u>Afectarea fluxului sanguin prin monitorizare</u></p> <p>12 săptămâni – 0/12 (0%)</p> <p>24 de săptămâni – 0/12 (0%)</p> <p>36 de săptămâni – 0/12 (0%)</p> <p>Măsurători ale tensiunii arteriale (3 oi – 36 de săptămâni)</p> <ul style="list-style-type: none"> <li>Nu s-a detectat o reducere importantă a fluxului sanguin</li> </ul> <p>Date macroscopice pentru integrare și degradare (gradul 0-4)</p> <p><u>Locuri de abord carotidian</u></p> <p>Partea internă</p> <p>-încapsulare</p> <p>12 săptămâni 1,3</p> <p>24 de săptămâni 0,8</p> |

|  |  |  |  |  | 36 de săptămâni 0,7<br>-degradarea materialului<br>12 săptămâni 2,2<br>24 de săptămâni 2,3<br>36 de săptămâni 0,7<br><i>Partea externă</i><br>-incapsulare<br>12 săptămâni 2,0<br>24 de săptămâni 1,0<br>36 de săptămâni 0,8<br>-degradarea materialului<br>12 săptămâni 2,0<br>24 de săptămâni 2,7<br>36 de săptămâni 3,2<br><br><u>Locuri de abord femural</u><br><i>Partea externă</i><br>-incapsulare<br>12 săptămâni 1,0<br>24 de săptămâni 2,7<br>36 de săptămâni 1,0<br>-degradarea materialului<br>12 săptămâni 2,0<br>24 de săptămâni 2,4<br>36 de săptămâni 3,0<br><br><i>Partea internă</i><br>-incapsulare<br>12 săptămâni 2,0<br>24 de săptămâni 1,2<br>36 de săptămâni 1,0<br>-degradarea materialului<br>12 săptămâni 1,0<br>24 de săptămâni 2,2<br>36 de săptămâni 3,0<br><br><u>Date histologice pentru integrare, degradare și parametri inflamatori (media valorilor relevante, indice 0-4)</u><br>n=6<br><br><u>Locuri de abord carotidian</u><br>Fibroză externă<br>12 săptămâni – 2,3<br>24 de săptămâni – 2,3<br>36 de săptămâni – 1,8<br>Neointimă internă<br>12 săptămâni – 3,0<br>24 de săptămâni – 2,7<br>36 de săptămâni – 3,3 |
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|  |  |  |  |  | <p>Degradarea materialului</p> <p>12 săptămâni – 1,7</p> <p>24 de săptămâni – 3,0</p> <p>36 de săptămâni – 3 +</p> <p>Parametri inflamatori (macrofage)</p> <p>12 săptămâni – 3,0</p> <p>24 de săptămâni – 1,7</p> <p>36 de săptămâni – 1,7</p> <p><u>Locuri de abord femural</u></p> <p>Fibroză externă</p> <p>12 săptămâni – 1,3</p> <p>24 de săptămâni – 1,5</p> <p>36 de săptămâni – 1,7</p> <p>Neointimă internă</p> <p>12 săptămâni – 3,7</p> <p>24 de săptămâni – 3,3</p> <p>36 de săptămâni – 3,8</p> <p>Degradarea materialului</p> <p>12 săptămâni – 2,0</p> <p>24 de săptămâni – 3,0</p> <p>36 de săptămâni – 3+</p> <p>Parametri inflamatori (macrofage)</p> <p>12 săptămâni – 3,5</p> <p>24 de săptămâni – 1,8</p> <p>36 de săptămâni – 1,8</p> <p><u>Valori de permeabilitate histomorfologică</u></p> <p>Locuri de abord carotidian</p> <p>12 săptămâni 74,0%</p> <p>24 de săptămâni 81,9%</p> <p>36 de săptămâni -89,43%</p> <p>Locuri de abord femural</p> <p>12 săptămâni – 42,2%</p> <p>24 de săptămâni – 73,21%</p> <p>36 de săptămâni – 78,71%</p> <p><u>Permeabilitatea vaselor sanguine la ultrasunete (medie procentuală)</u></p> <p>Loc de abord carotidian</p> <p>12 săptămâni 94,6%</p> <p>24 de săptămâni – 96,7%</p> <p>36 de săptămâni – 94,7%</p> <p>Locuri de abord femural</p> <p>12 săptămâni – 66,9%</p> <p>24 de săptămâni – 63,6%</p> <p>36 de săptămâni – 75,1%</p> |
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|                                                                                                                                                                                                                                                                        |                                                                                |                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                           | <ul style="list-style-type: none"> <li>Nu s-a detectat niciun semn de intoleranță locală semnificativă (absența leziunilor inflamatorii, necrotice sau degenerative vizibile) la 12, 24 sau 36 de săptămâni</li> <li>Nu s-a înregistrat nicio reacție tisulară adversă semnificativă asociată cu gazda și dispozitivul</li> <li>Degradarea implantului a fost aproape completă la 36 de săptămâni</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002</p> <p>Radi Medical System AB</p> <p>Efectuat de Biomatech, Franța</p> | <p>Studiu pe animale</p> | <p>Scopul studiului a fost evaluarea biocompatibilității și biofuncționalității unui implant biodegradabil conceput pentru realizarea hemostazei în sistemul vascular. Dispozitivul testat a fost destinat introducerii în orificiul de puncție al arterelor pentru realizarea hemostazei. Un disc a pătruns în orificiul de puncție din arteră, iar celălalt a strâns discul interior din exteriorul arterei. Ambele discuri au fost introduse printr-o teacă a setului introdus. Discurile au fost concepute pentru a preveni sângerarea, a se vindeca în peretele vasului și, în cele din urmă, a se degrada și a fi resorbite. Studiul a fost conceput pentru a colecta și analiza date după implantarea funcțională la oi și porci pentru a evalua capacitatea implantului de a menține funcția fiziologică atunci când este utilizat în sistemul circulator, a determina răspunsul gazdei și reacția dispozitivului (integritate</p> | <p>Perioada de implantare/monitorizare este de 5 săptămâni pentru toate animalele</p> <p>4 oi, 1 porc</p> <p>14 elemente de închidere</p> <p>8 elemente de închidere implantate în 2 oi,</p> <p>2 elemente de închidere implantate în 1 porc</p> <p>Când au fost implantate două elemente de închidere în aceeași arteră femurală, acestea au fost implantate la o distanță &gt;30 mm</p> | <p>Au fost înregistrate criteriile pentru orice semne adverse (inflamație, necroză, hemoragie sau orice altă leziune) sau pentru formarea oricărui strat pseudo-intima subțire. O atenție deosebită a fost acordată integrării tisulare inițiale a dispozitivului, cu accent special pe încapsularea discului interior.</p> <p>La nivel macroscopic, nu au fost observate semne semnificative de intoleranță locală sau formare de trombi. Observarea macroscopică nu a evidențiat nicio diferență între oi sau porc după implantarea elementelor de închidere în arterele femurale. La nivel macroscopic, nu au fost observate semne semnificative de intoleranță locală sau formare de trombi. Observarea macroscopică nu a evidențiat nicio diferență între oi sau porc după implantarea elementelor de închidere în arterele femurale.</p> |

|  |  |  | fizică, încapsulare tisulară (la sacrificare) și a evalua degradarea implantului |  | <p>Analiza histopatologică a locului de implantare la oi nu a evidențiat reacții adverse locale. Discul interior și cel exterior au prezentat semne de degradare și, în unele cazuri, s-au rupt în bucăți mai mici. Discurile interioare s-au resorbit complet în țesutul neointimal. La porc, analiza histopatologică a indicat semne ușor mai puternic inflamatorii în jurul discurilor interioare și exterioare. La ambele animale, filamentul multiplu a prezentat semne ușor mai puternic inflamatorii decât materialul discului, lucru normal pentru firele de sutură împletite, din cauza întinderii mai mari a suprafeței.</p> <p>Permeabilitatea vasului sanguin a fost măsurată după 5 săptămâni utilizând trei metode diferite, histomorfometric, histomorfometric în combinație cu măsurarea diametrului vasului sanguin prin utilizarea șublerului și prin utilizarea ultrasonografiei Doppler color. Permeabilitatea medie a vasului sanguin la oi a fost între 60 și 80%, în funcție de metodă (12 observații). La porc, permeabilitatea vasului sanguin a fost între 40 și 80% (2 observații).</p> |
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| Primul studiu clinic pe oameni                                                                                                                                                                               |                                  |                                                 |                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
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| Denumirea studiului                                                                                                                                                                                          | Anul/Investigator<br>coordonator | Tipul<br>studiului                              | Obiective                                                                                                                                                                                                                                                                                                                    | Repere                                                                                                                                                                                                                                                                                                                                                                              | Criterii pentru posibila<br>acceptare                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB     | Studiu deschis, cu un singur braț, multicentric | Obiectivele studiului au fost determinarea siguranței, performanței și eficacității FemoSeal Vascular Closure System (sistemul FemoSeal) în general și, în mod specific, ale elementelor de închidere, la pacienții supuși procedurilor cardiologice de diagnosticare și intervenționale utilizând abordul arterial femural. | Studiu format din 2 părți<br><br>n total = 80<br>n partea 1 = 20<br>n partea 2 = 60<br><br>Indicații:<br><br>Partea 1 – cateterizarea cardiacă de diagnosticare utilizând artera femurală ca loc de abord<br><br>Partea 2 – pacienții supuși procedurilor cardiologice de diagnosticare și intervenționale utilizând artera femurală ca loc de abord<br><br>Monitorizare 30 de zile | Rezultate<br><br><u>-hemostază realizată cu FS fără compresie</u><br><br>- Partea 1 20/20 (100%)<br>- Partea 2 58/60 (97%)<br><br>Timp median până la hemostază la momentul procedurii (partea 2) – 1,0 minute (interval imediat – 8 minute)<br><br><u>Timp până la mobilizare postoperatorie (minute)</u><br><br>Partea 1 –<br>Mediană: 33,0<br>mediu: 67,8<br><br>Partea 2 –<br>mediană: 45<br>mediu: 87,5<br><br><u>Incidența complicațiilor vasculare majore – monitorizare 30 de zile</u><br><br>Partea 1<br>-Fără complicații vasculare 20/20 (100%)<br><br>Partea 2<br>Pseudoanevrism – 1/59 (1,69%)<br><br><u>Eșecul tratamentului</u><br><br>Partea 1 – 0/20 (0%)<br><br>Partea 2 – 3/60 (5%)<br><ul style="list-style-type: none"><li>2 din cauza imposibilității de realizare a hemostazei fără utilizarea compresiei</li><li>1 din cauza complicațiilor vasculare majore, pseudoanevrism</li></ul> |

|  |  |  |  |  | <u>Supurare persistentă</u><br>Partea 1 – 0/20 (0%)<br>Partea 2- 8/60 (13%)<br><br><u>Hematom</u><br>Partea 1 – 0/20 (0%)<br>Partea 2 – 6/60 (10%) |
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Ca parte a planului de dezvoltare anterior introducerii pe piață pentru FemoSeal™ VCS, au fost finalizate 3 teste funcționale pe animale. În 2000, înainte de inițierea studiilor clinice, s-a efectuat un studiu pe animale pentru evaluarea biofuncționalității FemoSeal™ VCS. Acest studiu a evaluat capacitatea elementelor de închidere de a menține funcția fiziologică și de a evalua degradarea acesteia. La 18 luni, materialul discului interior și exterior nu mai era vizibil, fiind înlocuit cu un țesut fibros endoluminal. În concluzie, a fost confirmată capacitatea elementului de închidere FemoSeal™ VCS de a menține funcția fiziologică atunci când este utilizat în sistemul circulator.

În 2002 s-a efectuat un studiu pe animale pentru evaluarea biocompatibilității și biofuncționalității unui implant biodegradabil FemoSeal™ VCS, conceput pentru realizarea hemostazei în sistemul vascular. Pe scurt, degradarea implantului a fost aproape completă până la 36 de săptămâni și nu a existat nicio reacție tisulară adversă semnificativă.

Un alt studiu efectuat pe animale în 2002 a evaluat biocompatibilitatea și biofuncționalitatea unui implant biodegradabil, FemoSeal™ VCS, conceput pentru a realiza hemostaza în sistemul vascular. După 5 săptămâni, încapsularea discului a fost completă și au fost observate semne de degradare la discurile interne și externe. În concluzie, a fost confirmată capacitatea implantului de a menține funcția fiziologică atunci când este utilizat în sistemul circulator.

Ca parte a planului de dezvoltare clinică pentru FemoSeal™ VCS, Radi Medical System AB a efectuat o investigație clinică anterioară introducerii pe piață. Această investigație clinică nu este publicată sau disponibilă online. Studiul pentru dispozitivul modelul # 1200 a fost efectuat în 2002-2004 în conformitate cu standardul european EN 540 (investigațiile clinice efectuate pe dispozitive medicale, pentru subiecți umani) și în conformitate cu considerentele generale ICH privind studiile clinice și ghidul privind bunele practici clinice. Detaliile acestui studiu sunt prezentate în raportul EU-SE-001. Studiul clinic a fost prezentat în raportul final al Radi Medical Systems AB, „Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures”. Studiul clinic a fost efectuat cu primul model #11200 de FemoSeal™ și s-a concentrat asupra siguranței

și eficacității componentelor de închidere implantabile. Singura diferență dintre primul model #11200 și modelul actual, C11202, este dimensiunea în French, 6 F și respectiv 7 F, precum și sistemul îmbunătățit de introducere. Beneficiile clinice, utilizarea preconizată, principiile de operare și materiile prime ale elementelor de închidere implantabile, garniturii interioare și discului de blocare exterior rămân neschimbate.

Utilizarea preconizată a dispozitivului se aplica pacienților supuși procedurilor cardiologice de diagnosticare sau intervenționale, utilizând artera femurală drept punct de abord. Obiectivul acestui studiu a fost acela de a determina siguranța, performanța și eficacitatea FemoSeal™ VCS. A fost un studiu prospectiv, multicentric, cu un singur braț, deschis, cu o monitorizare de 30 de zile.

Criteriul principal de evaluare a performanței a fost timpul până la hemostază definit ca absența sângerării abundente. Criteriul principal de evaluare a siguranței a fost incidența complicațiilor vasculare majore pe parcursul a 30 de zile. Criteriile secundare de evaluare au inclus timpul până la mobilizare postoperatorie, proporția de eșecuri ale tratamentului, incidența evenimentelor adverse și caracteristicile de performanță ale dispozitivului în timpul introducerii și utilizării.

Pacienții incluși în acest studiu au fost adulți capabili să își dea consimțământul informat și cu cel puțin o pulsație periferică intactă la nivelul arterelor periferice. Pacienții au fost excluși din studiu dacă prezentau oricare dintre următoarele afecțiuni:

- Antecedent de boală vasculară periferică
- Boală autoimună
- Boală hemoragică cunoscută cu anemie severă
- INR >1,5
- Infarct miocardic în ultimele 72 de ore
- Hipertensiune necontrolată, în ciuda tratamentului
- Obezitate care împiedică abordul cu tehnica Seldinger
- Prezența grefei vasculare sau a stentului la locul arteriotomiei
- Puncție ipsilaterală anterioară în ultimele 3 luni
- Speranță de viață < 6 luni

În plus, pacienții au fost examinați intraoperatoriu și excluși din studiu dacă s-a observat oricare dintre următoarele:

- Diametrul lumenului arterei femurale comune < 5 mm
- Ramuri arteriale la 2 cm proximal față de locul puncției
- Stenoză semnificativă la 3 cm față de locul puncției

- Utilizarea tecii setului introducător principal > 6 Fr
- Puncție la bifurcația femurală sau distal față de aceasta
- Puncții femurale multiple
- Puncție cunoscută sau suspectată a peretelui femural posterior
- Hematom de dimensiuni mari (2:6 cm) la finalizarea procedurii
- Introducere dificilă a tecii primare pentru procedură, din cauza țesutului sau vasului sanguin sinuos

Acest studiu cu un singur protocol a fost efectuat în două părți: În timpul Părții 1 s-au înrolat 20 de pacienți, apoi s-a realizat o analiză privind siguranța, iar apoi s-au înrolat încă 60 de pacienți în timpul Părții 2.

În Partea 1, vârsta medie a pacienților înscriși a fost 65,9 ani, 70,0% dintre pacienți au fost bărbați, iar 95% dintre pacienți primeau medicamente concomitente. În Partea 2 a studiului, vârsta medie a fost de 63,8 ani, 78% au fost bărbați și 100% primeau medicamente concomitente.

Pacienții supuși procedurilor de cateterizare cardiacă de diagnosticare (Partea 1 și Partea 2) sau intervenționale (Partea 2) au fost eligibili pentru înrolarea în studiu. Procedurile au fost în conformitate cu standardul de îngrijire la fiecare dintre spitalele participante, urmate de utilizarea FemoSeal™ VCS. Datele pacienților au fost colectate la vizita inițială, în timpul procedurii și la 1 zi și 30 de zile după procedură. Rezultatele sunt sintetizate în **Tabelul 1.5** și indică faptul că FemoSeal™ VCS este sigur și eficient pentru utilizarea la această populație de pacienți.

**Tabelul 1.5 Rezultatele clinice raportate în studiul anterior introducerii pe piață**

|                                                                                                              | Partea 1    | Partea 2                 |
|--------------------------------------------------------------------------------------------------------------|-------------|--------------------------|
| Număr de pacienți                                                                                            | 20          | 60                       |
| Timp mediu până la hemostază                                                                                 | 1,2 minute  | 1,6 minute <sup>a</sup>  |
| Timp mediu până la mobilizare postoperatorie                                                                 | 72,2 minute | 87,5 minute <sup>b</sup> |
| Incidența complicațiilor vasculare majore <sup>c</sup>                                                       | 0 (0%)      | 1 (2%)                   |
| Număr de pacienți cu evenimente adverse                                                                      | 5 (25%)     | 19 (32%)                 |
| Eșecul tratamentului (definit drept complicații vasculare majore, necesitatea compresiei manuale sau ambele) | 0 (0%)      | 3 (5%)                   |
| Defecțiuni ale dispozitivului                                                                                | 0 (0%)      | 6 (10%)                  |

*<sup>a</sup>Pe baza dimensiunii totale a lotului de 58, deoarece la 2 pacienți nu s-a realizat hemostaza la momentul procedurii din cauza puncțiilor ipsilaterale anterioare. La acești pacienți, hemostaza a fost realizată la 7 minute și 37 de minute.*

*<sup>b</sup>Pe baza unei dimensiuni totale a lotului de 59: 1 pacient nu a fost inclus deoarece a fost trecut pe ventilator din cauza edemului pulmonar și nu a putut fi mobilizat timp de peste o săptămână.*

*<sup>c</sup>Definite drept complicații vasculare care necesită transfuzie de sânge sau reparație chirurgicală, sau infecție locală care necesită administrarea de antibiotice, spitalizare sau prelungirea spitalizării sau debridarea locului*

Nu au fost observate complicații vasculare majore în Partea 1 a studiului. În Partea 2 a studiului a fost raportată 1 complicație vasculară majoră: pseudoanevrism care a fost raportat în decurs de 1 zi după procedură. Evenimentul a necesitat compresia ghidată ecografică și o injecție cu trombină în pseudoanevrism, prelungind spitalizarea pacientului.

Dintre cele 5 evenimente adverse raportate în Partea 1 a studiului, a existat 1 eveniment advers posibil asociat dispozitivului: un eveniment minor de sângerare abundentă la 1 zi după procedură. Dintre cele 19 evenimente adverse raportate în Partea 2 a studiului, au fost observate 3 evenimente adverse minore de hematom asociate dispozitivului și s-au observat 6 evenimente minore posibil asociate dispozitivului, inclusiv 3 raportări de supurare persistentă, 2 de hematoame și 1 de durere de picior după exerciții fizice.

3 pacienți au fost considerați eșecuri ale tratamentului în Partea 2: 2 din cauza eșecului de a realiza hemostaza fără utilizarea compresiei și 1 din cauza complicației vasculare majore (pseudoanevrism). Nu au existat eșecuri ale tratamentului în Partea 1 a studiului.

Dintre cele șase defecțiuni ale dispozitivului în Partea 2 a studiului, trei nu au afectat procedura, una a fost atribuită erorii utilizatorului, una a fost scurgerea setului introdus și una a fost o articulație ruptă a filamentului. Ultimele două probleme au fost soluționate prin actualizări ale modelului implementate la C11202.

Partea 2 a studiului clinic anterior introducerii pe piață nu a raportat rezultatele urmăririi la 6 luni din cauza lipsei de complianță a pacienților. Rezultatele la 30 de zile ale studiului clinic anterior introducerii pe piață (EU-SE-001), în conformitate cu perioada de urmărire din literatura clinică, demonstrează că FemoSeal™ VCS este sigur și eficient.

#### **1.4.2 Rezumatul datelor din studiile clinice ulterioare introducerii pe piață**

Au existat 4 studii clinice ulterioare introducerii pe piață finalizate, descrise în **Tabelul 1.6** de mai jos. Aceste investigații clinice nu sunt publicate sau disponibile online.

**Tabelul 1.6 Studii clinice ulterioare introducerii pe piață, finalizate**

| Studii clinice ulterioare introducerii pe piață, finalizate                                    |                                                                    |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|------------------------------------------------------------------------------------------------|--------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------|----|-----|----------|-------|----------|-----------|----|-----------|-----------|-------------------------|----------|--------------------|------------|---------------------|-----------|-------------------|---------|-----------------------|----------|--------------------------------|----------|----------------------|-----------|--------------------------|-----------|-----------------------------------|----------|----------------------|--------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Denumirea studiului                                                                            | Anul/Investigator coordonator                                      | Tipul studiului                                                                                  | Obiective                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Repere                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Criterii pentru posibila acceptare                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)<br>User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI                                                       | Studiu ulterior introducerii pe piață, Gradul de acceptare de către utilizatori a noului ambalaj | Studiu ulterior introducerii pe piață efectuat asupra actualizării modelului de FemoSeal Vascular® Closure System #11202, care are un sistem de introducere modificat comparativ cu primul model, #11200, pentru a documenta funcționalitatea.<br><br>Obiectivul studiului a fost acela de a primi feedback cu privire la Instrucțiunile de utilizare (IDU) revizuite și la proiectul de instruire pentru medici și asistente medicale, de a confirma evaluările efectuate în analiza de risc și de a oferi informații cu privire la orice îmbunătățire a calității produsului. | 100 de pacienți<br><ul style="list-style-type: none"><li>63 de bărbați/37 de femei</li><li>Vârsta medie 68 de ani pentru femei, 65 de ani pentru bărbați</li></ul><br>2 spitale suedeze, 6 medici<br><br>112 dispozitive<br><br>Date achiziționate în formularele cu fișele medicale (CRF)<br><br>Timp de observație planificat – 30 de minute de la momentul aplicării                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Rezultate<br><br>1. Ilustrațiile/Instrucțiunile din IDU au fost considerate informative și adecvate<br><br>2. Hemostază imediată (91/100) |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)              | Dr. Nicolas Moes, Universitatea de Medicină din Innsbruck, Austria | Evaluarea de confirmare ulterioară introducerii pe piață                                         | Obiectivul acestui studiu a fost acela de a evalua siguranța și performanța FemoSeal® utilizat în timpul rutinei clinice normale la pacienții supuși procedurii de cateterizare cardiacă de diagnosticare sau procedurii intervenționale cardiace percutanate efectuate cu o teacă 7 F.                                                                                                                                                                                                                                                                                         | 50 de pacienți consecutivi<br><br>Indicație – cateterizare cardiacă de diagnosticare sau invazivă din artera femurală comună<br><br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.6±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                         | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.6±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Criterii finale principale de evaluare<br><ul style="list-style-type: none"><li>Criterii principale de evaluare a eficacității – TTH (timpul până la hemostază) cu sau fără supurare, dar fără compresie suplimentară, manuală sau mecanică.</li><li>Criterii de evaluare a siguranței – incidența evenimentelor adverse – complicații vasculare minore și majore și toate celelalte evenimente adverse – grave și minore pe durata studiului (mai exact, până la externarea pacientului).</li></ul><br>Rezultate<br><ul style="list-style-type: none"><li>Timp mediu până la hemostază</li><li>Diagnosticare – 56,6 ± 29 secunde</li><li>Intervențional 59,9 ± 16,2 secunde</li></ul> |
| n                                                                                              | 50                                                                 |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| men                                                                                            | 35 (70%)                                                           |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| women                                                                                          | 15 (30%)                                                           |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| PCI cases                                                                                      | 15                                                                 |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| age (yrs)                                                                                      | 62.6±11.1                                                          |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| body mass index (kg/m²)                                                                        | 25.4±6.7                                                           |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| systolic BP (mmHg)                                                                             | 131.2±20.9                                                         |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| diastolic BP (mmHg)                                                                            | 77.9±10.6                                                          |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| diabetes mellitus                                                                              | 9 (18%)                                                            |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| arterial hypertension                                                                          | 34 (68%)                                                           |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| previous coronary intervention                                                                 | 13 (26%)                                                           |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| preprocedure aspirin                                                                           | 50 (100%)                                                          |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| preprocedure clopidogrel                                                                       | 50 (100%)                                                          |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Procedural unfractionated heparin                                                              | 15 (30%)                                                           |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Procedural abciximab                                                                           | 2 (4%)                                                             |                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                           |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |



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|                                                                                                                                 |                                 |                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                          | <ul style="list-style-type: none"> <li>• Toți pacienții 57,8 ±26,3</li> <li>• Toți pacienții au putut fi mobilizați după 4 ore de odihnă la pat, fără niciun fel de problemă.</li> </ul> <p>Rezultate în materie de siguranță</p> <ul style="list-style-type: none"> <li>• 49/50 (98%) fără complicații vasculare până la externare</li> <li>• Timp mediu până la externare 2,6 zile</li> <li>• 1/50 (2%) sângerare minoră în ziua următoare după o mobilizare fără evenimente în ziua angiografiei</li> </ul>                                                                                                                             |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | 2009 RADI                       | Studiu ulterior introducerii pe piață                                   | <p>Studiul ar trebui să stabilească dacă utilizatorii/clientii au perceput orice tip de problemă cu noul ambalaj, în special cu partea exterioară nesterilă a pungii Tuvek/PET-PE.</p> <p>De asemenea, studiul ar trebui să stabilească dacă medicul curant percepe vreo diferență în ceea ce privește etapele de introducere/utilizare a dispozitivului în comparație cu dispozitivele utilizate anterior.</p> <p>De asemenea, studiul ar trebui să ofere informații privind posibilele nevoi suplimentare de îmbunătățire a calității produsului.</p> | <p>25 de dispozitive</p> <p>4 spitale suedeze</p> <p>16/25 (64%) dintre pacienți au fost pacienți cu ICP (intervenție coronariană percutanată) cu medicamente anticoagulante puternice</p>                                                                                                                                               | <p>Rezultate</p> <ol style="list-style-type: none"> <li>1. Probleme în legătură cu ambalajul – 21/25 (84%) de introduceri au reușit; 4/25 (16%) nu au reușit (1 – testarea noului set introdus, 1 disc interior a trecut prin arteriotomie la pasul de revenire, butonul a ieșit și discul exterior a fost introdus în canalul tisular de incizie, 2 hemostaza imediată nu a fost realizată în ciuda lipsei problemelor de aplicare.)</li> <li>2. Hemostaza imediată la 19/25 (76%) pacienți</li> <li>3. Sângerare 11/25 (44%) – 9/25 (36%) supurare/hemoragie, 2/25 (8%) hematoame</li> </ol> <p>Frecvență totală a evenimentelor 19%</p> |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022) | 2022/Terumo Medical Corporation | Prospectiv, multicentric, observațional, ulterior introducerii pe piață | De a demonstra în continuare siguranța și eficacitatea FemoSeal™ VCS în realizarea hemostazei la locul de abord al arterei femurale comune (CFA) la subiecți supuși procedurilor endovasculare percutanate într-un cadru clinic real                                                                                                                                                                                                                                                                                                                    | <ul style="list-style-type: none"> <li>• Monitorizarea pacientului la 30 de zile (± 7 zile) prin vizită la spital sau apel telefonic.</li> <li>• Înscriere: Din decembrie 2021 până în iulie 2022.</li> <li>• 230 de subiecți înscriși care sunt supuși procedurilor endovasculare de diagnostic sau de intervenție în cadrul</li> </ul> | <ul style="list-style-type: none"> <li>• <b>Date demografice/comorbidități:</b></li> <li>- Sex: 161 bărbați (70%)/69 femei (30%).</li> <li>- Vârsta medie: 70 ± 12.</li> <li>- IMC: 26,1 ± 4,95 kg/m<sup>2</sup>.</li> <li>- Hipertensiune arterială: 160 pacienți (69,6%).</li> <li>- Dislipidemie: 128 (55,7%).</li> </ul>                                                                                                                                                                                                                                                                                                               |

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|  |  |  | <p>căroră se utilizează FemoSeal™.</p> <p>3 centre europene: Franța (92 de pacienți), Germania (38 de pacienți), Belgia (100 de pacienți).</p> | <p>- Boală arterială coronariană: 42 (18,3%).</p> <p>- Fumător în prezent: 86 (37,6%).</p> <p>- Fost fumător: 66 (28,8%).</p> <p>- Boală coronariană: 34 (14%).</p> <p>- Istoric de infarct miocardic: 18 (7,8%).</p> <p>- Revascularizarea arterelor periferice 12 (5,2%) artera carotidă și 83 (37,5%) artera membrelor inferioare.</p> <p>- Terapie antiplachetară (la vizita inițială): 211 (91,7%), inclusiv 21 (9,1%) terapie antiplachetară dublă (DAPT).</p> <p>- Anticoagulare orală: 40 (17,4%) pacienți.</p> <p>• <b>Caracteristicile intervenției:</b></p> <p>- Mediu: clinic cu internare 162 cazuri (70,4%), clinic ambulatoriu 68 cazuri (29,6%).</p> <p>- Indicație predominantă: claudicație 147 cazuri (63,9%).</p> <p>- Abord: 35 anterograd (15,3%), 194 retrograd (84,7%).</p> <p>• <b>Criterii finale principale</b></p> <p>- Siguranța combinată (absența complicațiilor majore la nivelul membrului la locul de abord în decurs de 6 ore după procedură) și criteriul final de eficacitate (hemostaza reușită la locul puncției) obținute la 215/226 (95,1%) [Î 95%: 91,46; 97,55] de pacienți în setul de analize complete și 215/230 (93,5%) [Î 95% 89,47, 96,30] în setul tratat cu FemoSeal™.</p> <p>- Criteriul final al eficacității a fost atins la 219/226 (96,9%) Î [93,7, 98,7] de pacienți.</p> |
|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|--|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <p>- Criteriu final de siguranță atins la 220/230 (95,2%) [Î 95%: 92,15, 97,90] de pacienți.</p> <p>• <b>Criterii finale secundare:</b></p> <p>- Absența complicațiilor minore la locul de abord în decurs de șase ore după procedură a fost obținută la 225/230 (97,8%) [Î 95%: 95,00; 99,29].</p> <p>- Absența complicațiilor majore și minore la locul de abord de la șase ore până la 30 de zile după procedură a fost obținută la 219/230 (95,2%) [Î 95%:91,60; 97,59] de pacienți.</p> <p>- Timp mediu până la hemostază cu FemoSeal™ VCD: 0,42 (0,25; 0,50) minute.</p> <p>- Timp mediu până la mobilizare postoperatorie: 5,00 (4,54; 5,50) minute.</p> <p>- Durată medie de spitalizare: 23,98 (22,72, 25,00) ore.</p> <p>- Ușurința în utilizare a FemoSeal™ VCS: „ușor” sau „foarte ușor” de implantat în 98,7% din cazuri („ușor” de implantat în 21 (9,2%), „foarte ușor” de implantat în 205 (89,5%)), cu rezistență zero sau scăzută la implantare în 226 (98,3%) de cazuri.</p> <p>152/230 (66,1%) de pacienți tratați cu firul de ghidaj inclus în kitul FemoSeal™ (GW 0,038”) și recomandat în FemoSeal™ fără deficiențe ale dispozitivului sau evenimente adverse raportate.</p> |
|--|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Studiul din 2006 a fost efectuat pentru a confirma siguranța și eficacitatea dispozitivului actual cu un sistem de introducere îmbunătățit și pentru a obține feedback privind instrucțiunile de utilizare și programul de instruire pentru FemoSeal™ VCS. Studiul a inclus 100 de pacienți și criteriul principal de evaluare a fost dacă s-a realizat hemostaza sau dacă au fost necesare compresii manuale sau mecanice suplimentare. Acest studiu a concluzionat că introducerea FemoSeal™ VCS a reușit în majoritatea cazurilor (în 91% dintre cazuri s-a realizat hemostaza imediată).

Studiul din 2008 a înregistrat 50 de pacienți pentru a evalua siguranța și performanța FemoSeal™ VCS la utilizarea în timpul rutinei clinice normale la pacienții supuși cateterizării cardiace cu o teacă de 7 Fr. Criteriul principal de evaluare a studiului a fost colectarea datelor privind timpul până la hemostază și timpul până la mobilizare postoperatorie fără compresie suplimentară, manuală sau mecanică. Rezultatele studiului au concluzionat că timpul mediu până la hemostază a fost de 57,8 secunde, iar toți pacienții au fost mobilizați după 4 ore de odihnă la pat.

Studiul din 2009 s-a referit la evaluarea noului ambalaj al FemoSeal™ VCS. În studiu au fost înscrși 25 de pacienți. Criteriul principal de evaluare a fost dacă utilizatorul a întâmpinat probleme cu ambalajul. Utilizatorii nu au observat nicio problemă privind noul ambalaj al FemoSeal™ VCS. Acest studiu a colectat, de asemenea, date privind timpul până la hemostază.

Obiectivul studiului din 2022 a fost acela de a colecta în mod proactiv date legate de siguranța și eficacitatea FemoSeal VCS în realizarea hemostazei la locul de abord al arterei femurale comune (CFA) la subiecți supuși procedurilor endovasculare percutanate într-un cadru clinic real. În studiu au fost înscrși 230 de pacienți. Criteriile principale de evaluare pentru registru sunt succesul procedurii (mai exact, hemostaza reușită la locul puncției) și reducerea complicațiilor majore (de exemplu, leziune vasculară, sângerare asociată locului de abord, infecție la locul de abord, compresie manuală repetată și ischemie acută ipsilaterală la nivelul picioarelor, legată de locul de abord). Studiul a concluzionat că FemoSeal™ VCS are performanțe bune în medii reale și asigură o hemostază eficientă și rate scăzute de complicații la locul de abord pentru pacienții supuși intervențiilor endovasculare periferice. Acesta demonstrează o performanță bună, cu un timp scurt până la hemostază și un feedback bun al operatorului privind utilitatea, ceea ce face ca FemoSeal™ VCS să fie un dispozitiv valoros pentru închiderea abordului femural.

### **1.4.3 Rezumatul datelor din monitorizarea clinică ulterioară introducerii pe piață**

#### **1.4.3.1 Monitorizare clinică finalizată ulterioară introducerii pe piață**

Un rezumat al activităților de urmărire clinică ulterioare introducerii pe piață finalizate este descris în **Tabelul 1.7** de mai jos.

**Tabelul 1.7. Activități de monitorizare clinică ulterioară introducerii pe piață**

| Activități de monitorizare clinică ulterioară introducerii pe piață, finalizate |             |                                                             |                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|---------------------------------------------------------------------------------|-------------|-------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Denumirea activității                                                           | An/CI       | Tipul studiului                                             | Obiective                                                                                                                                                                                                                                                                                                         | Repere                                                                                                                                                                                                                                                                                                                                       | Criterii pentru posibila acceptare                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021)       | 2021<br>TMC | Sondaj clinic post-vânzare - sondaj privind înalta calitate | Sondaj post-vânzare pentru colectarea feedbackului prospectiv legat de utilizarea dispozitivului de închidere vasculară FemoSeal™ distribuit pe piețele Uniunii Europene.                                                                                                                                         | <ul style="list-style-type: none"> <li>120 de cazuri</li> <li>8 de medici unici cu &gt; 5 ani de experiență</li> <li>Mai multe țări din Europa</li> </ul>                                                                                                                                                                                    | <b>Evaluări ale dispozitivelor pe scala 1-5 – Declarații privind sondajul</b> <ul style="list-style-type: none"> <li>Criterii de acceptare <ul style="list-style-type: none"> <li>Evaluările 3-5 sunt considerate ca fiind favorabile</li> <li>Toate afirmațiile trebuie să aibă un feedback pozitiv ≥80%</li> </ul> </li> <li>Rezultate <ul style="list-style-type: none"> <li>Nicio declarație privind chestionarul nu a primit &gt;20% răspunsuri nefavorabile.</li> <li>Nu au fost înregistrate reclamații privind produsul</li> </ul> </li> </ul> |
| 20210298 – 0,035” and 0038” Guidewire Clinical Survey Report (2021)             | 2021<br>TMC | Sondaj clinic post-vânzare – sondaj privind înalta calitate | Chestionar ulterior introducerii pe piață pentru colectarea feedbackului prospectiv privind utilizarea firului de ghidaj de 0,035” inclus cu dispozitivul de închidere vasculară Angio-Seal™ VIP (VCD) de 6 Fr și a firului de ghidaj de 0,038” inclus atât cu Angio-Seal™ VIP VCD de 8 Fr, cât și cu sistemul de | <ul style="list-style-type: none"> <li>Chestionare pentru firul de 0,035” <ul style="list-style-type: none"> <li>106 sondaje</li> <li>64 de medici</li> </ul> </li> <li>Chestionare pentru firul de 0,038” <ul style="list-style-type: none"> <li>109 sondaje</li> <li>55 de medici</li> </ul> </li> <li>12 sondaje retrospective</li> </ul> | <b>Evaluări ale dispozitivelor pe scala 1-5 – Declarații privind sondajul</b> <ul style="list-style-type: none"> <li>Criterii de acceptare <ul style="list-style-type: none"> <li>Evaluările 3-5 sunt considerate ca fiind favorabile</li> <li>Toate afirmațiile trebuie să aibă un feedback pozitiv ≥80%</li> </ul> </li> <li>Rezultate <ul style="list-style-type: none"> <li>Toate firele de ghidare au primit evaluări acceptabile</li> <li>Nu au fost depuse reclamații privind produsul</li> </ul> </li> </ul>                                   |

| Activități de monitorizare clinică ulterioară introducerii pe piață, finalizate                                                 |                     |                                                             |                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|---------------------------------------------------------------------------------------------------------------------------------|---------------------|-------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                 |                     |                                                             | închidere vasculară FemoSeal distribuit pe piețele din Uniunea Europeană.                                                 |                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024<br>TMC/TE | Sondaj clinic post-vânzare - sondaj privind înalta calitate | Pentru a colecta în mod prospectiv feedback legat de utilizarea FemoSeal™ VCS cu fire de ghidare distribuite pe piața UE. | <ul style="list-style-type: none"> <li>126 sondaje <ul style="list-style-type: none"> <li>7 locații</li> <li>5 țări</li> </ul> </li> <li>14 noiembrie 2023 - 11 iunie 2024</li> <li>Specialitatea medicului: <ul style="list-style-type: none"> <li>Chirurgie vasculară</li> <li>Radiologie intervențională</li> <li>Angiologie</li> </ul> </li> </ul> | <b>Evaluări ale dispozitivelor pe scala 5 – Declarații privind sondajul</b> <ul style="list-style-type: none"> <li>Criterii de acceptare <ul style="list-style-type: none"> <li>Evaluările 3-5 sunt considerate ca fiind favorabile</li> <li>Toate afirmațiile trebuie să aibă un feedback pozitiv <math>\geq 80\%</math></li> <li>Dacă apar evenimente adverse în cadrul acestui sondaj, acestea trebuie să fie cele anticipate de managementul riscurilor.</li> </ul> </li> <li>Date demografice privind pacienții <ul style="list-style-type: none"> <li>Femei: 29,4% (37/126)</li> <li>Bărbați: 69,8% (88/126)</li> <li>Sex nedezevăluit: 0,8 (1/126)</li> <li>Vârsta &gt;75 ani: 31,7%</li> </ul> </li> <li>Rezultate <ul style="list-style-type: none"> <li>Firul de ghidare furnizat împreună cu FemoSeal™ VCS: 101/126 (80,2%).</li> <li>Durata procedurii (minute): 63,4 (36,6) (medie</li> </ul> </li> </ul> |

| Activități de monitorizare clinică ulterioară introducerii pe piață, finalizate |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|---------------------------------------------------------------------------------|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                 |  |  |  |  | <p>(SD)); 57,0<br/>(36,0-81,0)<br/>(medie (IQR))</p> <ul style="list-style-type: none"> <li>○ Toate evaluările performanței FemoSeal™ VCS au fost favorabile.</li> <li>○ Toate evaluările firelor de ghidare furnizate de FemoSeal™ VCS au fost favorabile.</li> <li>○ Un (0,8%) eveniment advers: discurile FemoSeal™ VCS nu au fost bine aliniate, probabil din cauza utilizării unui fir de ghidaj rigid (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 inch) care a necesitat compresie manuală pentru a se obține hemostaza.</li> </ul> |

Terumo Medical Corporation a finalizat trei sondaje privind înalta calitate în rândul utilizatorilor medici în perioada de raportare curentă (1 septembrie 2019 - 31 august 2024).

Studiile clinice pentru FemoSeal™ au colectat date clinice proactive în ceea ce privește siguranța și performanța FemoSeal™ VCS în timpul utilizării clinice. Studiul a inclus întrebări axate pe dispozitivul general și accesoriile asociate, inclusiv firul de ghidaj de 0,038" și interacțiunile directe ale acestora. Studiile clinice pentru firul de ghidaj au colectat date clinice proactive în ceea ce privește siguranța și performanța în timpul utilizării clinice a firului de ghidaj de 0,038" furnizat împreună cu FemoSeal™ VCS. Întrebările din studiu s-au concentrat în mod specific pe utilizarea generală a firului de ghidaj, de la introducerea prin teaca procedurală în vasculatură până la scoaterea firului.

Firele de ghidaj FemoSeal™ VCS și 0,038" incluse cu dispozitivul au primit toate evaluări acceptabile iar șase (6) reclamații au fost depuse pentru dispozitiv și nouă (9) non-reclamații pentru firul de ghidaj pe baza evaluării comentariilor primite din studiile clinice de înaltă calitate. Reclamațiile au fost evaluate atât pentru FemoSeal, cât și pentru firul de ghidaj, și au fost evaluate ca parte a procesului Terumo de urmărire ulterioară introducerii pe piață. Nu au fost identificate riscuri și/sau niveluri de risc noi.

În 2024, ca parte a activităților PMCF, a fost finalizat un sondaj la utilizatorii medici. Rezultatele sondajului au demonstrat că evaluarea performanței și siguranței FemoSeal™ VCS au fost în general foarte favorabile. Compatibilitatea altor fire de ghidare decât cel standard furnizat împreună cu FemoSeal™ VCS a fost, de asemenea, demonstrată.

#### **1.4.3.2 Urmărire clinică ulterioară introducerii pe piață în curs/planificată**

TMC are o activitate de monitorizare clinică ulterioară introducerii pe piață în curs/planificată. Se va realiza un studiu clinic pentru a colecta în mod prospectiv feedback legat de utilizarea firului de ghidaj cu FemoSeal VCS distribuit pe piața UE. Studiul va fi completat de medici pentru a studia care sunt firele de ghidaj utilizate în timpul procedurii. Scopul acestui sondaj este de a aborda o lacună identificată ca fiind lipsa literaturii de specialitate și a comentariilor revizorului extern cu privire la compatibilitatea FemoSeal™ VCS cu utilizarea altor fire de ghidare de la alte mărci decât Terumo. Feedbackul include rezultatele tehnice, performanța clinică și siguranța în ceea ce privește performanța dispozitivului cu diferite fire de ghidaj.

#### **1.4.4 Rezumatul datelor din analiza sistematică a literaturii de specialitate**

Terumo Medical Corporation desfășoară revizuri sistematice ale literaturii de specialitate pentru a colecta și evalua date privind siguranța și performanța clinică din studii publicate despre FemoSeal™ VCS și/sau dispozitive similare. Scopul examinării anuale a literaturii de specialitate publicate este de a identifica reacții adverse necunoscute anterior, de a monitoriza reacțiile adverse cunoscute, de a identifica riscurile emergente și de a identifica posibila utilizare necorespunzătoare sistematică sau utilizare în alte indicații decât cele menționate a FemoSeal™ VCS.

Cea mai recentă analiză sistematică a literaturii de specialitate, care a acoperit perioada 1 septembrie 2019 - 31 august 2024, a identificat 29 de studii publicate care au furnizat date privind siguranța și performanța clinică a dispozitivului FemoSeal™ VCS. Douăzeci și trei de referințe au raportat utilizarea FemoSeal™ VCS conform indicațiilor menționate, iar utilizarea în afara indicațiilor menționate a fost raportată în nouă studii. În general, analiza literaturii de specialitate asociată studiilor specifice utilizării FemoSeal™ VCS indică o populație de studiu reprezentativă pentru pacienții din UE supuși procedurilor de cateterizare vasculară percutanată. Consultați **Secțiunea 3** pentru o listă a acestor 23 de publicații revizuite de omologi în care utilizarea a avut loc conform indicațiilor menționate.



Performanța clinică a fost evaluată prin următoarele măsurători:

- Timpul până la hemostază este mai bun decât sau comparabil cu stadiul actual al tehnicii pentru închiderea percutanată a arterei femurale comune.
- Timpul până la mobilizarea postoperatorie este mai bun decât sau comparabil cu stadiul actual al tehnicii pentru închiderea percutanată a arterei femurale comune.
- Rata complicațiilor postoperatorii este comparabilă cu sau mai redusă decât cea menționată pentru tratamentele standard actuale.

Pe baza acestor măsurători ale performanței clinice, datele din această analiză a literaturii de specialitate au indicat că FemoSeal™ VCS poate fi utilizat cu succes la închiderea puncției arteriale femurale (arteriotomie) la pacienții care au fost supuși cateterizării percutanate utilizând o teacă procedurală de 7 Fr sau mai mică. Hemostaza completă a fost obținută la majoritatea pacienților (79,65-100%) din cazuri și a fost asociată cu un timp mediu până la hemostază de 0,5 minute, timp mediu până la externare de 3 zile. Între 69,2 și 86,7% dintre pacienți au reușit să se deplaseze la 5 ore după închidere, cu o durată medie de repaus postoperatoriu de 349 min. Eșecul FemoSeal™ VCS a fost observat în 3,68-4% dintre cazuri, iar compresia manuală suplimentară a fost necesară în 0,9-4,4% dintre proceduri.

Siguranța clinică a fost evaluată în funcție de evenimentele adverse, inclusiv, dar fără a se limita la:

- Sângerare
- Hematom
- Pseudoanevrism
- Echimoză
- Fistulă arteriovenoasă
- Infecție
- Deces

Pentru fiecare dintre aceste evenimente adverse, frecvența raportată pentru FemoSeal™ VCS în studiile incluse a fost mai mică sau comparabilă cu cele raportate anterior pentru compresia manuală și alte dispozitive de închidere vasculară.

La examinarea a 10 rapoarte de caz nu au fost identificate evenimente adverse, deoarece nu au fost identificate riscuri noi, neanticipate, emergente sau inacceptabile.

Eficacitatea generală a utilizării FemoSeal™ VCS în timpul angiografiei de diagnostic sau al intervențiilor chirurgicale depinde de mai mulți factori, cum ar fi: sexul, vârsta, anatomia pacientului, comorbiditățile, amplasarea anatomică a locului puncției, experiența chirurgului, metoda de amplasare a VCD, îngrijirea postoperatorie, etc. Pe lângă succesul tehnic, inclusiv

obținerea hemostazei, FemoSeal™ VCS a oferit beneficii clinice în ceea ce privește închiderea vasculară după puncția arterială femurală, cum ar fi reducerea timpului până la hemostază, reducerea timpului până la mobilizare. Rezultatele privind performanța dispozitivului FemoSeal™ VCS sunt în concordanță cu cele preconizate pentru acest tip de dispozitiv atunci când este utilizat conform destinației. Unele dintre referințele obținute în timpul perioadei de căutare curente au arătat utilizarea dispozitivului vizat într-o altă locație anatomică decât artera femurală comună și pentru închiderea arteriotomiei >7 Fr, care este considerată a fi în afara indicațiilor menționate.

În timpul revizuirii nu au fost identificate efecte secundare necunoscute, riscuri emergente sau posibile utilizări necorespunzătoare sistematice ale dispozitivului. Cu toate acestea, dacă FemoSeal™ VCS este utilizat cu atenție de către medici instruiți, dispozitivul medical funcționează ca un dispozitiv clinic util și necesar. În general, terapia-țintă și, prin urmare, FemoSeal™ VCS abordează nevoia clinică existentă în prezent în tratamentul complicațiilor asociate accesului vascular.

În general, datele din această analiză a literaturii de specialitate nu au identificat nicio problemă de performanță sau de siguranță în mediul clinic care să nu fi fost cunoscută anterior sau efecte adverse care să fi avut loc cu frecvențe mai mari decât cele anticipate/acceptabile. Prin urmare, din această analiză a literaturii de specialitate se poate concluziona că FemoSeal™ VCS, atunci când este utilizat pentru a asigura compresia pentru hemostază la arteriotomie după cateterizarea percutanată, continuă să funcționeze conform așteptărilor și nu este asociat cu evenimente grave în materie de siguranță.

#### **1.4.5 Rezumatul datelor din supravegherea ulterioară introducerii pe piață**

Este implementat un sistem PMS proactiv și o analiză a tuturor reclamațiilor este efectuată lunar și în conformitate cu procedurile interne de producție. Datele privind reclamațiile au fost analizate în perioada 1 septembrie 2019 - 31 august 2024. În total au existat 28 de rapoarte de vigilență privind dispozitivele medicale (MDV) și 476 de rapoarte cu reclamații ale clienților trimise producătorului. Dintre cele 28 de rapoarte MDV, 27 au fost asociate cu evenimente adverse și unul cu funcționarea defectuoasă a dispozitivului. Au existat două decese în perioada de raportare, dar niciunul dintre decesele raportate nu a fost considerat a fi asociat cu dispozitivul vizat. Dintre cele 476 de reclamații adresate producătorului, cele mai frecvente motive pentru reclamații au fost dificultățile de amplasare (146 de apariții, rata de apariție de 0,0142%). Modul de eroare al evenimentelor de extragere este al doilea cel mai frecvent, cu o rată de 0,0126% (130 evenimente).

FemoSeal™ Vascular Closure System a fost comercializat în 1.053.639 de unități la nivel global și 827.833 în Spațiul Economic European. Frecvența calculată a reclamațiilor raportate la vânzările globale este de 0,046%. Rata totală de reclamații ale clienților este foarte scăzută. Nu au fost identificate riscuri noi care să nu fie incluse în Instrucțiunile de utilizare și în documentația privind riscurile.

Frecvențele de apariție a efectelor secundare nedorite sunt prezentate în **Tabelul 1.2**. În rândul reclamațiilor nu au fost identificate riscuri noi neanticipate, emergente sau inacceptabile. Nu au existat creșteri semnificative ale frecvenței sau severității reacțiilor adverse cunoscute.

#### **1.4.6 Rezumatul general al caracteristicilor de performanță clinică și siguranță**

FemoSeal™ VCS este indicat pentru utilizarea la închiderea puncției arteriale femurale comune (arteriotomie) la pacienții care au fost supuși cateterizării percutanate utilizând o teacă procedurală de 7 F (2,33 mm) sau mai mică. Această evaluare clinică se bazează pe o analiză cuprinzătoare a datelor clinice și a literaturii de specialitate disponibile anterior și ulterior introducerii pe piață relevante pentru utilizarea prevăzută a FemoSeal™ VCS.

A fost efectuată o analiză complexă a literaturii de specialitate publicate în perioada 1 septembrie 2019 - 31 august 2024. Dovezile au inclus 29 de studii pentru FemoSeal™ VCS. Dovezile furnizate în cadrul evaluării clinice concluzionează că, atunci când este utilizat conform indicațiilor, dispozitivul vizat este sigur și eficient, iar orice riscuri sau reacții adverse nedorite care pot fi asociate cu dispozitivul în condiții normale de utilizare constituie riscuri acceptabile atunci când sunt analizate în raport cu beneficiile pentru pacient. Rezultatele privind performanța dispozitivelor vizate sunt în concordanță cu cele preconizate pentru acest tip de dispozitiv atunci când este utilizat conform destinației.

Potențialele reacții adverse nedorite asociate cu utilizarea FemoSeal™ VCS includ evenimentele adverse raportate în mod obișnuit cu mijloace alternative de închidere a arteriotomiei, de ex., sângerare și hematom. În general, frecvențele de apariție a evenimentelor adverse raportate în legătură cu utilizarea FemoSeal™ VCS sunt similare cu frecvențele raportate în cazul compresiei manuale și al dispozitivelor de închidere vasculară similare. În mod specific, pentru sângerare și hematom, frecvențele raportate pentru FemoSeal™ VCS sunt mai mici decât frecvențele raportate pentru dispozitivele de închidere vasculară similare. Fiecare eveniment advers raportat, atât din literatura de specialitate publicată, cât și din urmărirea ulterioară introducerii pe piață, fusese identificat anterior (consultați **Secțiunea 1.3**).

Datele existente privind siguranța și performanța clinică a FemoSeal™ VCS sugerează că beneficiile pacientului ca urmare a utilizării acestui dispozitiv de închidere vasculară depășesc riscurile posibile atunci când este utilizat în conformitate cu Instrucțiunile de utilizare.

După cum s-a arătat în secțiunile anterioare de mai sus, datele furnizate pentru FemoSeal™ VCS demonstrează consecvența dintre datele referitoare la dispozitivul evaluat (de exemplu, utilizarea dispozitivului, rezultatele privind siguranța, performanța clinică și beneficiile clinice), dispozitivele echivalente identificate și datele referitoare la dispozitivele similare enumerate în stadiul actual al tehnicii.

Analiza încrucișată a datelor de siguranță nu a identificat niciun fel de lacune între următoarele:

- datele menționate în stadiul actual al tehnicii;
- datele specifice dispozitivului în curs de evaluare;
- datele menționate în Fișierul(ele) de gestionare a riscurilor
- datele menționate pe etichetă și/sau în Instrucțiunile de utilizare (de exemplu, riscurile reziduale care trebuie transmise utilizatorului sunt abordate).

Siguranța clinică a fost demonstrată prin rate reduse de complicații, identificate în literatura clinică publicată, cu cercetări comparative, studii clinice sponsorizate de companie, revizuirea datelor ulterioare introducerii pe piață, asociate cu lipsa retragerilor de pe piață. Nu au fost identificate probleme cu privire la performanță; literatura de specialitate revizuită a inclus utilizarea dispozitivului FemoSeal™ VCS, care a fost în concordanță cu utilizarea prevăzută a producătorului.

### 1.5 Posibile alternative de diagnostic sau terapeutice

Compresia manuală este utilizată în mod tradițional pentru a realiza hemostaza la locul arteriotomiei după cateterizările vasculare. Compresia manuală a fost asociată cu imobilizarea pacientului perioade lungi de timp (până la 8 ore după o procedură) și cu disconfort substanțial și șederi prelungite în spital. În cadrul unei analize sistematice recente, s-a constatat că timpul median pentru realizarea hemostazei cu compresie manuală a fost de 20,8 minute.<sup>1</sup>

Alternativele la compresia manuală includ dispozitive hemostatice externe care aplică compresie mecanică la locul arteriotomiei. Aceste dispozitive nu scurtează timpul până la hemostază sau timpul până la mobilizare postoperatorie, ci reduc necesarul de personal prin înlocuirea compresiei manuale cu compresia mecanică. Frecvențele evenimentelor adverse asociate cu utilizarea compresiei mecanice sunt similare cu frecvențele în cazul compresiei manuale.

Dispozitivele de închidere vasculară, cum ar fi FemoSeal™ VCS, sunt concepute pentru a închide arteriotomia. Scopul acestora este de a reduce timpul până la hemostază și de a permite mobilizarea postoperatorie timpurie. În cadrul unei analize sistematice recente care a inclus 13 dispozitive disponibile pe piață, s-a constatat că timpul median pentru obținerea hemostazei cu un dispozitiv de închidere vasculară este de 5,4 minute. Timpul mediu de hemostază pentru dispozitivele individuale de închidere vasculară a variat de la 1 minut (FemoSeal™ VCS) la 14 minute, majoritatea dispozitivelor înregistrând între 4 și 10 minute.<sup>1</sup>

Evenimentele adverse raportate frecvent asociate cu închiderea locului arteriotomiei cu compresii manuale, dispozitive hemostatice externe sau dispozitive de închidere vasculară includ hematom, sângerare la locul de abord, pseudoanevrism, fistulă arteriovenoasă și infecție. În cadrul aceleiași analize sistematice (34 de studii randomizate și controlate, 14.401 pacienți), s-a constatat că ratele evenimentelor adverse sunt similare între compresia manuală și utilizarea

dispozitivelor de închidere vasculară, cu excepția faptului că hemoragia a avut tendința de a fi puțin mai mare cu dispozitivele de închidere vasculară.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Profil de utilizator și instruire recomandate

Utilizatorii propuși ai FemoSeal™ Vascular Closure System sunt medici cu instruire care îi califică pentru efectuarea abordului arterial și a închiderii pentru procedurile endovasculare prin artera femurală comună și care au participat la programul de instruire pentru medici al Terumo Medical Corporation FemoSeal™.

## 1.7 Standarde armonizate și comune relevante

| Referință standard | Anul curent de conformitate/Rev | Descriere                                                                                                                                |
|--------------------|---------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070          | 2014/AMD1:2018                  | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070       | 2014/A1:2018                    | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance       | 20 mai 2021                     | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052         | 2015                            | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213         | 2017                            | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503         | 2020                            | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182         | 2019                            | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |

| Referință standard | Anul curent de conformitate/Rev | Descriere                                                                                                                                                                |
|--------------------|---------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 13485       | 2016/A11:2021                   | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 13485          | 2016                            | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 14644-1        | 2015                            | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1     | 2015                            | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2        | 2015                            | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2     | 2015                            | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3        | 2019                            | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3     | 2019                            | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1        | 2003                            | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1     | 2003                            | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2        | 2003/TC1:2004                   | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |

| Referință standard           | Anul curent de conformitate/Rev | Descriere                                                                                                                                     |
|------------------------------|---------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 14698-2               | 2003/TC 1:2004                  | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| USP <788>                    | N/A                             | Particulate Contamination: Sub-Visible Particles                                                                                              |
| Farmacopeea europeană 2.9.19 | N/A                             | Contaminare cu particule: Particule sub limita vizibilității cu ochiul liber                                                                  |
| IEC 62366-1                  | 2015                            | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN 62366-1                   | 2015                            | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN ISO 14971                 | 2019/A11:2021                   | Medical devices — Application of risk management to Medical devices                                                                           |
| ISO 14971                    | 2019                            | Medical devices — Application of risk management to Medical devices                                                                           |
| ASTM F1980                   | 2016                            | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                                           |
| EN ISO 10993-1               | 2020                            | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                    |
| ISO 10993-1                  | 2018                            | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                    |
| EN ISO 10993-2               | 2006                            | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                                                |
| ISO 10993-2                  | 2006                            | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                                                |
| EN ISO 10993-3               | 2014                            | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity                          |
| ISO 10993-3                  | 2014                            | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity                          |



| Referință standard | Anul curent de conformitate/Rev | Descriere                                                                                                      |
|--------------------|---------------------------------|----------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-4     | 2017                            | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood               |
| ISO 10993-4        | 2017                            | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood               |
| EN ISO 10993-5     | 2009                            | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                             |
| ISO 10993-5        | 2009                            | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                             |
| EN ISO 10993-6     | 2016                            | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                  |
| ISO 10993-6        | 2016                            | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                  |
| EN ISO 10993-10    | 2023                            | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                 |
| ISO 10993-10       | 2021                            | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                 |
| EN ISO 10993-11    | 2018                            | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                |
| ISO 10993-11       | 2017                            | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                |
| EN ISO 10993-12    | 2021                            | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                 |
| ISO 10993-12       | 2021                            | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                 |
| EN ISO 10993-17    | 2009                            | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances |
| ISO 10993-17       | 2002                            | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances |



| Referință standard | Anul curent de conformitate/Rev | Descriere                                                                                                                                                                    |
|--------------------|---------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-18       | 2020/A1:2022                    | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-18    | 2020/A1:2022                    | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-23    | 2021                            | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23       | 2021                            | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382         | 2018                            | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756          | 2017                            | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>           | N/A                             | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>          | N/A                             | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72     | 2019                            | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135       | 2014/A1:2019                    | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135          | 2014/A1:2018                    | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |

| Referință standard | Anul curent de conformitate/Rev | Descriere                                                                                                                                                       |
|--------------------|---------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-7     | 2008/A1:2022                    | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                       |
| ISO 10993-7        | 2008/A1:2019                    | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                               |
| EN 556-1           | 2024                            | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices |
| EN ISO 11737-1     | 2018/A1:2021                    | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11737-1        | 2018/A1:2021                    | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| EN ISO 11138-1     | 2017                            | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-1        | 2017                            | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| EN ISO 11138-2     | 2017                            | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 11138-2        | 2017                            | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| EN ISO 15223-1     | 2016                            | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| ISO 15223-1        | 2016                            | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| EN 1041            | 2008/A1:2013                    | Information supplied by the manufacturer of medical devices                                                                                                     |

| Referință standard | Anul curent de conformitate/Rev | Descriere                                                                                                                                                                  |
|--------------------|---------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 11607-1     | 2020/A1:2023                    | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| ISO 11607-1        | 2019/A1:2023                    | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| EN ISO 11607-2     | 2020/A1:2023                    | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ISO 11607-2        | 2019/A1:2023                    | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169         | 2016                            | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M  | 2016                            | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825         | 2018                            | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096         | 2011 (R 2019)                   | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M      | 2015                            | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24       | 2021                            | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3        | 2020                            | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |
| MDCG 2020-8        | 2020                            | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                             |

| Referință standard | Anul curent de conformitate/Rev | Descriere                                                                                                                                                                                                                                                     |
|--------------------|---------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-7        | 2020                            | Post-market clinical follow-up (PMCF) Plan Template<br>A guide for manufacturers and notified bodies                                                                                                                                                          |
| MDCG 2020-6        | 2020                            | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                                                                                                          |
| MDCG 2019-9<br>v1  | 2022                            | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                                                                                      |
| MDCG 2019-8<br>v2  | 2020                            | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15       | 2020                            | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11       | 2021                            | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19       | 2021                            | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1<br>v4  | 2021                            | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2        | 2019                            | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1        | 2019                            | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7        | 2018                            | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6        | 2018                            | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device                                                                                                                                                                |

| Referință standard     | Anul curent de conformitate/Rev | Descriere                                                                                                                                                                                     |
|------------------------|---------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                        |                                 | Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                                                  |
| MDCG 2018-4            | 2018                            | MDCG 2018-4 Annex: UDI database<br>Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                               |
| MDCG 2018-3<br>v1      | 2020                            | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25           | 2021                            | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2.12-2<br>Rev 2 | 2012                            | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                        |

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### 3.0 ISTORICUL REVIZUIRILOR

| Numărul revizuirii SSCP     | Data emiterii    | Descrierea modificării                                          | Revizuire validată de organismul notificat                                                                                                                                                                                                                                                                                                                            |
|-----------------------------|------------------|-----------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022                | 20 ianuarie 2023 | Ediția inițială, la certificarea CE MDR                         | <p><input checked="" type="checkbox"/> Da</p> <p>Limba de validare: English</p> <p><input type="checkbox"/> Nu (valabil numai pentru dispozitivele implantabile din clasa IIa sau IIb (MDR, articolul 52 (4) alineatul 2) pentru care SSCP nu este încă validat de ON)</p> <p><input type="checkbox"/> Altele (explicați):</p>                                        |
| SSCP-FS-2023 – Revizuirea 1 | 15 martie 2024   | Actualizat pentru perioada 1 ianuarie 2019 - 31 decembrie 2023. | <p><input checked="" type="checkbox"/> Da</p> <p>Limba de validare: English</p> <p><input type="checkbox"/> Nu (valabil numai pentru dispozitivele implantabile de clasă IIa sau unele dispozitive implantabile de clasă IIb (MDR, articolul 52 (4) alineatul 2) pentru care SSCP nu este încă validat de ON)</p> <p><input type="checkbox"/> Altele (explicați):</p> |
| SSCP-FS-2024 Revizuirea 1   |                  | Actualizat pentru perioada 1 ianuarie 2019 - 31 decembrie 2024. | <p><input type="checkbox"/> Da</p> <p>Limba de validare: English</p> <p><input type="checkbox"/> Nu (valabil numai pentru dispozitivele implantabile de clasă IIa sau unele dispozitive implantabile de clasă IIb (MDR, articolul 52 (4) alineatul 2) pentru care SSCP nu este încă validat de ON)</p> <p><input type="checkbox"/> Altele (explicați):</p>            |

|                              |               |                                                           |                                                                                                                                                                                                                                                                                                                                                                                  |
|------------------------------|---------------|-----------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>Revizuirea 2 | June 20, 2025 | Revizuit pe baza<br>interogărilor NSAI<br>pentru validare | <input checked="" type="checkbox"/> Da<br><br>Limba de validare: English<br><br><input type="checkbox"/> Nu (valabil numai pentru<br>dispozitivele implantabile de<br>clasă IIa sau unele dispozitive<br>implantabile de clasă IIb<br>(MDR, articolul 52 (4) alineatul<br>2) pentru care SSCP nu este<br>încă validat de ON)<br><br><input type="checkbox"/> Altele (explicați): |
|------------------------------|---------------|-----------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

**Сводная информация о безопасности и клинических характеристиках**

**FemoSeal™ Vascular Closure System**

|                                                                                            |                                                                                                       |
|--------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|
| <b>Производитель</b>                                                                       | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 USA (США)             |
| <b>SRN производителя</b>                                                                   | US-MF-000019594                                                                                       |
| <b>Представитель руководства/ответственный за соблюдение нормативных требований (PRRC)</b> | Кимберли Фейтл (Kimberly Feitl)<br>Vice President, Quality                                            |
| <b>Базовый UDI-DI</b>                                                                      | 38970FS79                                                                                             |
| <b>Номер EMDN</b>                                                                          | C900199 – Системы гемостаза – Прочее                                                                  |
| <b>Класс устройства</b>                                                                    | Класс III                                                                                             |
| <b>Год выпуска первого устройства с маркировкой CE</b>                                     | 2005                                                                                                  |
| <b>Представитель в ЕС</b>                                                                  | Terumo Europe N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgium (Бельгия)<br>SRN: BE-AR-000001433 |
| <b>Уполномоченный орган</b>                                                                | NSAI<br>CE 0050                                                                                       |

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Настоящая сводная информация о безопасности и клинических характеристиках (SSCP) предназначена для предоставления общественности доступа к обновленному краткому описанию основных аспектов безопасности и клинических характеристик системы закрытия сосудов FemoSeal™ Vascular Closure System (VCS).

Сводная информация о безопасности и клинических характеристиках устройства, предназначенная для пользователей / медицинских работников, приведена в **разделе 1.0**.

## **1.0 СВОДНАЯ ИНФОРМАЦИЯ ДЛЯ ПОЛЬЗОВАТЕЛЕЙ / МЕДИЦИНСКИХ РАБОТНИКОВ**

Сводная информация не заменяет инструкцию по эксплуатации в качестве основного документа, обеспечивающего безопасное использование устройства, и не предназначена для предоставления диагностических или терапевтических рекомендаций предполагаемым пользователям или пациентам. Сводная информация не предназначена для замены обязательной информации, содержащейся в картах имплантата или других обязательных документах.

### **1.1 Предполагаемая область применения устройства**

#### **1.1.1 Область применения**

FemoSeal™ Vascular Closure System представляет собой медицинское устройство, предназначенное для закрытия артериальной пункции после чрескожной катетеризации через общую бедренную артерию.

#### **1.1.2 Показания к применению**

FemoSeal™ Vascular Closure System показана к применению при закрытии общей бедренной артериальной пункции (артериотомии) у пациентов, которым проводилась чрескожная катетеризация с использованием процедурного интродьюсера размером 7F (2,33 мм) или меньше.

#### **1.1.3 Противопоказания и/или ограничения**

FemoSeal™ Vascular Closure System противопоказана пациентам с артериотомией, при которой использовались интродьюсеры или устройства размером более 2,33 мм (7F).

#### **1.1.4 Целевые группы пациентов**

Безопасность и эффективность FemoSeal™ Vascular Closure System установлены у пациентов в возрасте 18 лет и старше, которым проводилась чрескожная катетеризация с использованием процедурного интродьюсера размером 7F (2,33 мм) или меньше.

#### **1.1.5 Особые группы пациентов**

Безопасность и эффективность FemoSeal™ Vascular Closure System не установлена для следующих групп пациентов:

- пациенты с предшествующим аутоиммунным заболеванием.
- пациенты, проходящие терапевтический тромболиз.
- пациенты с клинически значимым заболеванием периферических сосудов.

- пациенты с неконтролируемой гипертензией ( $> 220$  мм рт. ст. систолического давления или  $> 110$  мм рт. ст. диастолического давления).
- пациенты с нарушением кровотечения, включая тромбоцитопению ( $< 100\,000$  тромбоцитов) или анемию ( $Hgb < 10$  мг/дл).
- пациенты с внутренним просветом общей бедренной артерии менее 5 мм.
- пациенты с нарушениями функции почек и/или печени.
- пациенты с другими сопутствующими заболеваниями.
- группы пациентов определенного расового и/или этнического происхождения.
- пациенты с инфарктом миокарда в течение 72 часов.
- пациенты с сосудистым имплантатом или стентом в месте пункции.
- беременные или кормящие пациентки.
- Пациенты в возрасте до 18 лет.

### 1.1.6 Предполагаемые пользователи

Предполагаемыми пользователями FemoSeal™ Vascular Closure System являются врачи, прошедшие обучение и имеющие квалификацию для выполнения артериального доступа и закрытия при эндоваскулярных процедурах с использованием общей бедренной артерии, и принявшие участие в программе обучения врачей Terumo Medical Corporation FemoSeal™.

## 1.2 Описание устройства

### 1.2.1 Описание устройства

Система закрытия сосудов FemoSeal™ Vascular Closure System производства компании Terumo Medical Corporation (TMC) представляет собой рассасывающееся устройство для закрытия сосудов, предназначенное для достижения гемостаза бедренной артерии после чрескожной катетеризации через общую бедренную артерию.

Закрывающие элементы FemoSeal™ состоят из двух рассасывающихся полимерных дисков, внутреннего уплотнителя и наружного закрывающего диска, которые удерживаются вместе рассасывающейся многоволоконной шовной нитью, таким образом механически герметизируя артериотомию (см. **рис. 1.1** и **рис. 1.2**). После доставки через интродьюсер с конической оболочкой внешний закрывающий диск устанавливается на многоволоконный жгут шовного материала, что приводит к механическому закрытию места пункции между внутренним и внешним закрывающим диском. Внутреннее уплотнение и внешний закрывающий диск удерживаются на месте трением о



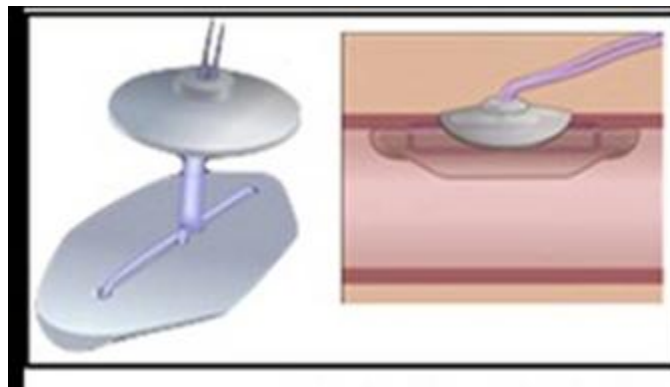
многоволоконный жгут. Гемостаз достигается механическим способом. Закрывающие элементы разлагаются в результате гидролиза.

Имплантируемые закрывающие компоненты, внутренний уплотнитель и внешний закрывающий диск разлагаются через восемнадцать (18) месяцев, в то время как многоволоконная шовная нить, по оценкам, разлагается и биоабсорбируется в результате гидролиза окружающей ткани через два (2) – три (3) года. Возможность поддержания сжатия имплантируемых закрывающих компонентов на артериотомии была проверена в течение восьми (8) часов. Продукты распада метаболизируются и выделяются с мочой или выводятся через легкие в виде углекислого газа. В исследованиях на животных эффекты накопления не наблюдались. Дополнительными компонентами FemoSeal™, контактирующими с живой тканью или кровью во время процедуры, являются интродьюсер с конической оболочкой, дилататор, закрывающая трубка, толкатель и проводник.

**Рис. 1.1 Внутреннее уплотнение и внешний закрывающий диск, соответственно**



**Рис. 1.2 Установлены внутреннее уплотнение и внешний закрывающий диск**

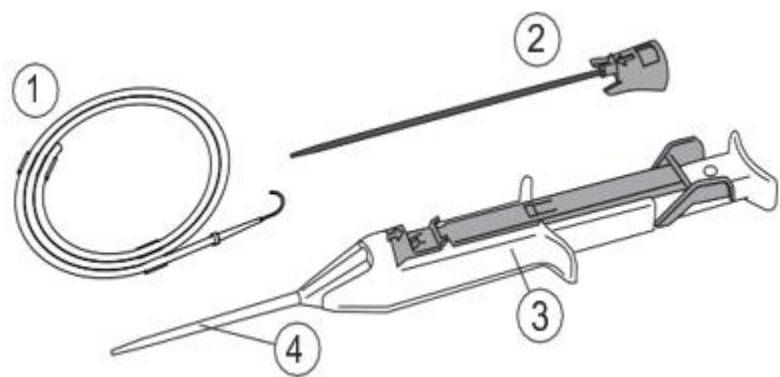


Устройство FemoSeal™ упаковано вместе с дилататором и проводником с наружным диаметром 0,038 дюйма (0,97 мм), длиной 27,5 дюйма (70 см) и J-образным кончиком, см.

**рис. 1.3** ниже. Проводник содержится в полиэтиленовой трубке. Все детали упакованы в прочный бумажный лоток. Упаковка также включает карту имплантата пациента.

FemoSeal™ Vascular Closure System не требует дополнительных принадлежностей для надлежащего функционирования. Устройство предназначено для использования только с дилататором и проводником, входящими в комплект поставки.

Рис. 1.3 Устройство FemoSeal™ VCS с проводником и дилататором



### 1.2.2 Сырьевые материалы и компоненты

В таблице 1.1 ниже перечислены компоненты системы FemoSeal™ VCS.

Таблица 1.1 Сырьевые материалы и компоненты системы FemoSeal™ VCS

| Номер детали | Описание                                                        |                                                                     | Материалы                                                                                                                                                                                 |
|--------------|-----------------------------------------------------------------|---------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1            | Проводник диаметром 0,038 дюйма (0,97 мм) с J-образным кончиком |                                                                     | Проводник: нержавеющая сталь 304<br><br>J-образный кончик: полипропилен, фиолетовый пигмент<br><br>Зажим: полиэтилен<br><br>Трубки: полиэтилен                                            |
| 2            | Дилататор FemoSeal                                              |                                                                     | Втулка: тетрагидрофуран, синий пигмент, полибутилентерефталат (PBT)<br><br>Трубка: полиэтилен высокой плотности (ПЭВП), черный пигмент<br><br>Смазочный материал: Силикон Dow Corning 360 |
| 3/4          | Устройство FemoSeal                                             | Литая деталь RD7 – внутреннее уплотнение и наружный стопорный диск* | Сополимер между гликолидом, триметиленкарбонатом, ε-капролактоном и ТМП: триметилпропаном (инициатором)                                                                                   |
|              |                                                                 | Многоволоконная нить *                                              | Сегментированный сополимер между L,L-лактидом, триметиленкарбонатом,                                                                                                                      |

|  |  |                                    |                                                                                                                                              |
|--|--|------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |                                    | ε-капролактоном и 1,3 пропандиолом (инициатором)<br><br>Покрытие представляет собой сополимер между гликолидом, ε-капролактоном и L-лизинном |
|  |  | Закрывающая трубка                 | Полипропилен                                                                                                                                 |
|  |  | Толкатель                          | Нержавеющая сталь 304V                                                                                                                       |
|  |  | Ползунок                           | Полибутилентерефталат (ПБТ)                                                                                                                  |
|  |  | Корпус                             | Полибутилентерефталат (ПБТ)                                                                                                                  |
|  |  | Кнопка                             | Полибутилентерефталат (ПБТ)                                                                                                                  |
|  |  | Крышка кнопки                      | Сополимер полиоксиметилена (ПОМ) / полиацеталя                                                                                               |
|  |  | Втулка                             | Полибутилентерефталат (ПБТ)                                                                                                                  |
|  |  | Прокладка                          | Полибутилентерефталат (ПБТ)                                                                                                                  |
|  |  | Конус                              | Полипропилен                                                                                                                                 |
|  |  | Крышка корпуса                     | Полибутилентерефталат (ПБТ)                                                                                                                  |
|  |  | Предохранительный фиксатор         | Полибутилентерефталат (РВТ), синий пигмент                                                                                                   |
|  |  | Крышка втулки                      | Полибутилентерефталат (ПБТ)                                                                                                                  |
|  |  | Уплотнительная прокладка трубки    | Силикон, твердость по Шору А 70                                                                                                              |
|  |  | Уплотнительная прокладка корпуса   | Силикон, твердость по Шору А 50                                                                                                              |
|  |  | Пружина                            | Нержавеющая сталь 302                                                                                                                        |
|  |  | Интродьюсер с конической оболочкой | Полипропилен<br><br>Силикон Dow Corning 360, гексан                                                                                          |

\* Имплантируемая часть устройства; имплантируемые компоненты не препятствуют проведению МРТ

Система FemoSeal™ VCS стерилизована этиленоксидом (ЭО) и является одноразовым медицинским устройством. Устройство FemoSeal™ VCS сконструировано таким образом, что его нельзя использовать повторно.

**Принцип действия**

Система FemoSeal™ VCS способствует механическому гемостазу путем размещения имплантируемых закрывающих элементов внутри и снаружи общей бедренной артерии. Механизм, предотвращающий кровотечение, обеспечивается внутренним уплотнением,

которое герметизирует место пункции, и внешним закрывающим диском, который удерживает внутренний уплотнитель на месте.

### 1.2.3 Клинические преимущества

Система FemoSeal™ VCS обеспечивает следующие клинические преимущества по сравнению с закрытием сосудов после пункции общей бедренной артерии:

- Сокращение времени до гемостаза<sup>1</sup>
- Сокращение времени до восстановления способности передвигаться<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

### 1.2.4 Предыдущие поколения или варианты

- Первая версия FemoSeal™ VCS (#11200) поступила на европейский рынок в 2005 году и частично в 2006 году.
- Актуальная система FemoSeal™ VCS (#11202) с улучшенной системой доставки представлена на рынке с 28 марта 2006 года.

### 1.2.5 Принадлежности, предназначенные для использования с устройством

Устройство FemoSeal™ поставляется в упаковке с дилататором с внешним диаметром 0,038 дюйма (0,97 мм) и проводником длиной 27,5 дюйма (70 см) и J-образным кончиком. Проводник является принадлежностью устройства FemoSeal™. J-образный кончик является компонентом проводника, а дилататор является компонентом устройства FemoSeal™. Проводник является единственной рассматриваемой принадлежностью. Проводник содержится в полиэтиленовой трубке. Все детали упакованы в прочный бумажный лоток. Упаковка также включает карту имплантата пациента. FemoSeal™ Vascular Closure System не требует дополнительных принадлежностей для надлежащего функционирования. Устройство предназначено для использования только с дилататором и проводником, входящими в комплект поставки.

### 1.2.6 Другие устройства и изделия, предназначенные для использования с устройством

Система FemoSeal™ VCS не требует дополнительных устройств для надлежащего функционирования.

### 1.3 Риски и предупреждения

#### 1.3.1 Остаточные риски и нежелательные последствия

Известные или предсказуемые нежелательные явления, вред и осложнения, связанные с использованием устройства Femo-Seal™ VCS в результате остаточного риска, перечислены в **таблице 1.2**. Частота возникновения основана на анализе документации по рискам и рассчитывается на основе данных послепродажных наблюдений с 1 сентября 2019 года по 31 августа 2024 года. Неизвестных остаточных рисков для FemoSeal™ VCS нет, и все применимые риски были рассмотрены в инструкции по эксплуатации и процессе управления рисками.

**Таблица 1.2. Неблагоприятные явления/осложнения с устройством FemoSeal**

| Вред                      | Частота возникновения (%) | Смягчающие факторы                                                                                                                                             |
|---------------------------|---------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Аллергическая реакция     | 0,0000                    | Меры и планы по максимально низкому риску были рассмотрены в рамках разработки продукта, производственных рекомендаций, маркировки продукта и обучения врачей. |
| Аневризма                 | 0,0000                    |                                                                                                                                                                |
| Артериовенозная фистула   | 0,0001                    |                                                                                                                                                                |
| Кровопотеря/кровотечение  | 0,0280                    |                                                                                                                                                                |
| Летальный исход           | 0,0002                    |                                                                                                                                                                |
| Экхимоз                   | 0,0000                    |                                                                                                                                                                |
| Эмболия                   | 0,0000                    |                                                                                                                                                                |
| Реакция на инородное тело | 0,0000                    |                                                                                                                                                                |
| Гематома                  | 0,0027                    |                                                                                                                                                                |
| Кровотечение              | 0,0001                    |                                                                                                                                                                |
| Инфекция                  | 0,0002                    |                                                                                                                                                                |
| Воспалительная реакция    | 0,0000                    |                                                                                                                                                                |
| Онемение                  | 0,0000                    |                                                                                                                                                                |
| Боль                      | 0,0000                    |                                                                                                                                                                |
| Дискомфорт пациента       | 0,0004                    |                                                                                                                                                                |
| Задержка процедуры        | 0,0065                    |                                                                                                                                                                |
| Псевдоаневризма           | 0,0004                    |                                                                                                                                                                |
| Забрюшинное кровотечение  | 0,0002                    |                                                                                                                                                                |

| Вред                                      | Частота возникновения (%) | Смягчающие факторы |
|-------------------------------------------|---------------------------|--------------------|
| Сепсис                                    | 0,0000                    |                    |
| Тромбоэмболия                             | 0,0000                    |                    |
| Тромбоз                                   | 0,0001                    |                    |
| Окклюзия сосуда/ишемия нижних конечностей | 0,0002                    |                    |
| Перфорация сосуда                         | 0,0000                    |                    |
| Рассечение/глубокий порез ткани сосуда    | 0,0003                    |                    |

### 1.3.2 Предупреждения и меры предосторожности

#### Предупреждения

1. Не используйте изделие, если упаковка повреждена или если не сохранена целостность стерильной барьерной системы.
2. Не используйте изделие после истечения срока годности – биоразлагаемые компоненты могут вести себя ненадлежащим образом.
3. Не используйте изделие, если какие-либо его элементы имеют признаки повреждения или неисправности.
4. Использование системы FemoSeal™ Vascular Closure System в тех случаях, когда возможно бактериальное загрязнение процедурного интродьюсера или окружающих тканей, может привести к инфицированию.
5. При подозрении на пункцию задней стенки артерии или пункцию нескольких артерий не полагайтесь исключительно на систему FemoSeal™ Vascular Closure System для достижения артериального гемостаза. Используйте дополнительное ручное или механическое сжатие.
6. Если место пункции находится на уровне или дистальнее бифуркации бедренной артерии, систему FemoSeal™ Vascular Closure System не следует использовать из-за риска неправильного размещения внутреннего уплотнителя. Это может привести к осложнениям кровотечения и/или нарушению нормального потока крови.
7. При наличии непрекращающегося артериального кровотечения из места разреза не разрезайте многоволоконную шовную нить до достижения гемостаза. Если гемостаз не достигается, зафиксируйте многоволоконную шовную нить стерильной повязкой для ран и примените дополнительное сжатие до достижения гемостаза. В

случае непрекращающегося артериального кровотечения могут возникнуть значительные геморрагические осложнения, которые могут привести к травмированию или смерти пациента.

8. Не используйте систему FemoSeal™ Vascular Closure System, если место пункции расположено проксимально относительно паховой связки, так как это может привести к забрюшинной гематоме.
9. Пациенты с повышенным риском кровотечения могут страдать от повышенной кровопотери, что потребует трансфузии.
10. Отсоединение внутреннего диска может привести к тромбозу и (или) эмболии.

### **Меры предосторожности**

1. Процедура установки системы FemoSeal™ Vascular Closure System должна выполняться врачами, прошедшими соответствующее обучение использованию устройства.
2. Выполните ограниченную бедренную ангиограмму или пункцию бедренной артерии под ультразвуковым контролем, прежде чем устанавливать систему закрытия сосудов FemoSeal™ Vascular Closure System.
3. Прекратите процедуру, если:
  - диаметр просвета общей бедренной артерии < 5 мм.
  - имеет место стеноз и (или) существенные бляшки вблизи места пункции общей бедренной артерии.
  - пункция артерии выполняется в месте бифуркации бедренной артерии или дистальнее него.
  - аномальные ветви или аномалии сосудов присутствуют вблизи места пункции общей бедренной артерии.
4. При наличии гематомы необходимо соблюдать особую осторожность при правильной установке интродьюсера с конической оболочкой в артерию.
5. Используйте методику одностенной пункции. Не выполняйте пункцию задней стенки артерии.
6. При использовании системы FemoSeal™ Vascular Closure System всегда соблюдайте стерильность.
7. Система FemoSeal™ Vascular Closure System предназначена только для одноразового использования и не должна повторно стерилизоваться или использоваться каким-либо образом. Устройство FemoSeal™ сконструировано таким образом, что его нельзя использовать повторно.

8. Если при установке внутреннего уплотнения возникает неожиданное сопротивление, прекратите процедуру.
9. Для правильного размещения внутреннего уплотнения переместите большой палец таким образом, чтобы кнопка могла свободно отскочить назад.
10. Перед установкой внешнего закрывающего диска убедитесь, что интродьюсер с конической оболочкой устройства FemoSeal™ находится под поверхностью кожи. У пациентов с небольшим расстоянием между бедренной артерией и уровнем кожи внешний закрывающий диск может случайно установиться выше уровня кожи.
11. Для правильного размещения может потребоваться надрез кожи перед установкой системы.
12. Если внутреннее уплотнение находится внутри артерии, но не удастся полностью нажать кнопку и установить внешний закрывающий диск, может потребоваться хирургическое вмешательство для удаления закрывающих элементов FemoSeal™.
13. Если в течение 18 месяцев будет необходимо выполнить повторную пункцию, ее следует выполнять по меньшей мере на один сантиметр проксимальнее предыдущего места доступа системы FemoSeal™ Vascular Closure System.
14. Попросите пациента следовать указаниям врача, касающимся осмотра места закрытия пункции.
15. Попросите пациента носить карту пациента с информацией о пациенте в течение следующих 18 месяцев

### **Меры предосторожности при выписке**

Перед рассмотрением вопроса о выписке оцените состояние пациента по следующим клиническим показаниям:

1. кровотечение и/или гематома в месте закрытия пункции.
2. Боль при ходьбе.
3. Признаки инфекции в месте закрытия пункции.

### **1.3.3 Корректирующие действия по эксплуатационной безопасности**

В период с 01 сентября 2019 г. по 31 августа 2024 г. в системе FemoSeal™ VCS было выполнено одно корректирующее действие по эксплуатационной безопасности.

В 2022 г. компания Terumo добровольно отозвала систему FemoSeal™ VCS из-за жалоб на сбой в технологическом процессе и тестировании выпуска партии изделия FemoSeal производства компании Elkton для измерения усилия прижима и усилия втягивания. В общей сложности из Южной Кореи было отозвано 950 единиц.



## 1.4 Клиническая оценка и послепродажный клинический контроль

**Таблица 1.3** включает список базовых исследований, включенных для вывода системы FemoSeal™ VCS на рынок, а также послепродажные исследования и послепродажный клинический контроль. Версия устройства, используемая в исследовании, включена в таблицу ниже. Первая версия FemoSeal™ VCS (#11200) появилась на рынке до 2006 года, а следующая версия (#C11202) была выпущена на рынок в 2006 году, именно она предлагается на рынке в настоящее время.

**Таблица 1.3 Сводная информация по базовым клиническим исследованиям**

| Предпродажное функциональное тестирование на животных                                                                                                                                                                                                                   | Версия устройства              |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                          |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                          |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                          |
| Первое клиническое исследование на людях                                                                                                                                                                                                                                |                                |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                          |
| Завершенные послепродажные клинические исследования                                                                                                                                                                                                                     |                                |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                                                                              | C11202<br>(текущее устройство) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                                                                                       | C11202<br>(текущее устройство) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                                                                                                                                                          | C11202<br>(текущее устройство) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)                                                                                                                                                  | C11202<br>(текущее устройство) |
| Планируемые/текущие послепродажные клинические исследования                                                                                                                                                                                                             |                                |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                                                                                                                                                              | C11202<br>(текущее устройство) |

| Послепродажный клинический контроль                                                                                             |                                |
|---------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(текущее устройство) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(текущее устройство) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(текущее устройство) |

### 1.4.1 Сводные данные предпродажных исследований на животных и клинических исследований

В **таблице 1.4** ниже описаны все предпродажные исследования, как на животных, так и клинические.

**Таблица 1.4. Сводные данные предпродажных исследований**

| Предпродажное функциональное тестирование на животных                                                                                                                                                                                                                   |                                                                                  |                                                  |                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|--------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Название исследования                                                                                                                                                                                                                                                   | Год / доверительный интервал (CI)                                                | Тип исследования                                 | Цели                                                                                                                                                                                                                                                          | Основные этапы                                                                                                                                                                                                                                                                                                                                                                                                                | Потенциальные критерии приемлемости                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 2000<br><br>Radi Medical System AB<br><br>Выполнено компанией Biomatech, Франция | Исследование на животных; поисковое исследование | Цель исследования заключалась в оценке биосовместимости и биофункциональности биоразлагаемого имплантата, предназначенного для достижения гемостаза в сосудистой системе. Адреса отчетов по резервным животным из исследования номер 862 (документ # 1051-01) | <p>N = 3 взрослых самки овцы, по 1 животному в каждый момент времени</p> <p>Отслеживание гистопатологического анализа, макроскопической сортировки по качеству и ультраструктурного анализа</p> <ul style="list-style-type: none"> <li>12 месяцев</li> <li>15 месяцев</li> <li>18 месяцев</li> </ul> <p>Контроль с цветовой ультразвуковой доплерографией – 30 дней в местах доступа к сонной артерии и бедренной артерии</p> | <p>Проходимость артерии</p> <ul style="list-style-type: none"> <li>Анализ потока крови после размещения устройства – уменьшение потока крови на 2/3, связанное с временным артериальным вазоспазмом, который был отнесен на счет процедуры; и то, и другое произошло на левой общей сонной артерии</li> <li>Цветовая ультразвуковая доплерография (4 недели) – 3/3 (100 %) без значительного сокращения потока крови через 30 дней после имплантации</li> </ul> <p>Макроскопические наблюдения</p> <ul style="list-style-type: none"> <li>12 месяцев – проходимость подтверждена</li> </ul> |

|  |  |  |  |  | <div> <div>макроскопически при отсутствии анатомически заметной окклюзии; отсутствие макроскопических повреждений, вызванных местной непереносимостью (геморрагия, некроз или неоваскуляризация); инкапсуляция внутреннего диска оказалась заметной</div> <div> <div>15 месяцев – макроскопическое наблюдение не выявило признаков воспаления; остатки внутренних или внешних дисков не выявлены; инкапсулирующая ткань, расположенная в области внешнего диска, имела тот же вид, что и при 12-месячным наблюдением</div> <div>18 месяцев – при макроскопическом наблюдении не выявлено признаков местной непереносимости, виден внешний диск (3/3 случая), деградация внутреннего диска завершена; 1/3 (левая общая сонная артерия) – в месте имплантации наблюдалось углубление стенки артерии (может быть связано с размещением устройства)</div> </div> <div> <div>Закключение</div> <div> <div>Макроскопически через 12, 15 и 18 месяцев после имплантации не было обнаружено никаких некротических, дегенеративных или тромботических признаков.</div> <div>Процесс деградации внутренних и наружных дисков продолжался в период от 12 до 18 месяцев и завершился через 18</div> </div> </div> </div> |
|--|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                                                                                                                                                                                                                                                                                |                                                                                  |                                                         |                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|---------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                                                                                                |                                                                                  |                                                         |                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                             | <p>месяцев;<br/>имплантированная область была покрыта беловатой тканью.</p> <ul style="list-style-type: none"> <li>Гистологически через 18 месяцев полимерный материал больше не был виден, но присутствовала эндолуминальная фиброзная ткань. Некротические, дегенеративные или тромбозные поражения не отмечались.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002 Radi Medical System AB</p> <p>Выполнено компанией Biomatech, Франция</p> | <p>Исследование на животных; поисковое исследование</p> | <p>Цель исследования заключалась в оценке биосовместимости биоразлагаемого имплантата, предназначенного для достижения гемостаза в сосудистой системе.</p> | <p>Последующий контроль (после имплантации)</p> <ul style="list-style-type: none"> <li>12 недель</li> <li>24 недели</li> <li>36 недель</li> </ul> <p>N = 12 овец, 3 животных в каждый момент времени, по 3 резервных животных были использованы через 12, 15 и 18 месяцев</p> <p>Места имплантации – правая и левая бедренные артерии, правая и левая общие сонные артерии</p> <p>Цветовая ультразвуковая доплерография</p> | <p><u>Проходимость сонных и бедренных артерий через 4 недели</u></p> <ul style="list-style-type: none"> <li>Уменьшение основного потока крови 0/12 (0 %)</li> </ul> <p><u>Значительного уменьшения потока крови не наблюдалось</u></p> <ul style="list-style-type: none"> <li>Сильное нарушение потока крови при введении устройства 0/12 (0 %)</li> <li>Уменьшение потока крови в левой общей сонной артерии 2/12 (16,6 %) из-за временного вазоспазма артерии (связанного с операцией, а не с устройством)</li> </ul> <p><u>Нарушение потока крови в ходе последующего контроля</u></p> <p>12 недель – 0/12 (0 %)<br/>24 недели – 0/12 (0 %)<br/>36 недель – 0/12 (0 %)</p> <p>Измерение кровяного давления (3 овцы – 36 недель)</p> <ul style="list-style-type: none"> <li>Не обнаружено значительное уменьшение потока крови</li> </ul> <p>Макроскопические данные по интеграции и деградации (класс 0-4)</p> |

|  |  |  |  |  | <div>Места на сонной артерии</div> <div>Внутренняя сторона</div> <div>-герметизация</div> <div>12 недель 1,3</div> <div>24 недели 0,8</div> <div>36 недель 0,7</div> <div>-разложение материала</div> <div>12 недель 2,2</div> <div>24 недели 2,3</div> <div>36 недель 0,7</div> <div>Внешняя сторона</div> <div>-герметизация</div> <div>12 недель 2,0</div> <div>24 недели 1,0</div> <div>36 недель 0,8</div> <div>-разложение материала</div> <div>12 недель 2,0</div> <div>24 недели 2,7</div> <div>36 недель 3,2</div> <div>Места на бедренной артерии</div> <div>Внешняя сторона</div> <div>-герметизация</div> <div>12 недель 1,0</div> <div>24 недели 2,7</div> <div>36 недель 1,0</div> <div>-разложение материала</div> <div>12 недель 2,0</div> <div>24 недели 2,4</div> <div>36 недель 3,0</div> <div>Внутренняя сторона</div> <div>-герметизация</div> <div>12 недель 2,0</div> <div>24 недели 1,2</div> <div>36 недель 1,0</div> <div>-разложение материала</div> <div>12 недель 1,0</div> <div>24 недели 2,2</div> <div>36 недель 3,0</div> <div>Гистологические данные по параметрам интеграции, деградации и воспалительных процессов (среднее из соответствующих значений, индекс 0-4) n=6</div> |
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|  |  |  |  |  | <u>Места на сонной артерии</u><br>Внешний фиброз<br>12 недель – 2,3<br>24 недели – 2,3<br>36 недель – 1,8<br>Внутренняя неоинтима<br>12 недель – 3,0<br>24 недели – 2,7<br>36 недель – 3,3<br>Разложение материала<br>12 недель – 1,7<br>24 недели – 3,0<br>36 недель – 3 +<br>Параметры воспаления (макрофаги)<br>12 недель – 3,0<br>24 недели – 1,7<br>36 недель – 1,7<br><u>Места на бедренной артерии</u><br>Внешний фиброз<br>12 недель – 1,3<br>24 недели – 1,5<br>36 недель – 1,7<br>Внутренняя неоинтима<br>12 недель – 3,7<br>24 недели – 3,3<br>36 недель – 3,8<br>Разложение материала<br>12 недель – 2,0<br>24 недели – 3,0<br>36 недель – 3+<br>Параметры воспаления (макрофаги)<br>12 недель – 3,5<br>24 недели – 1,8<br>36 недель – 1,8<br><u>Значения гистоморфологической проходимости</u><br>Места на сонной артерии<br>12 недель 74,0 %<br>24 недели 81,9 %<br>36 недель – 89,43 %<br>Места на бедренной артерии<br>12 недель – 42,2 %<br>24 недели – 73,21 %<br>36 недель – 78,71 % |
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| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002</p> <p>Radi Medical System AB</p> <p>Выполнено компанией Biomatech, Франция</p> | <p>Исследование на животных</p> | <p>Цель исследования состояла в оценке биосовместимости и биофункциональной возможности биоразлагаемого имплантата, предназначенного для достижения гемостаза в сосудистой системе. Испытанное устройство предназначалось для введения в отверстие для пункции в артериях с целью достижения гемостаза. Один диск вошел в отверстие для пункции артерии, а другой затянул внутренний диск снаружи артерии. Оба</p> | <p>Период имплантации / последующего наблюдения составляет 5 недель для всех животных</p> <p>4 овцы, 1 свинья</p> <p>14 закрывающих элементов</p> <p>8 закрывающих элементов, имплантированных на 2 овцах,</p> <p>2 закрывающих элемента, имплантированных на 1 свинье</p> | <p>Регистрировались любые признаки неблагоприятного воздействия (воспаление, некроз, кровоизлияние или любое другое повреждение) или образование тонкого псевдоинтимального слоя. Особое внимание было уделено первоначальной тканевой интеграции устройства с особым акцентом на инкапсуляцию внутреннего диска.</p> <p>При макроскопическом исследовании не наблюдалось</p>                                                                                                                                                                                                                                                                                                                                         |

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|  |  |  | <p>диска вводились через интродьюсер. Диски были разработаны для предотвращения кровотечения, заживления в стенке сосуда и, наконец, разложения и рассасывания. Исследование было разработано для сбора и анализа данных после функциональной имплантации на овцах и свиньях для оценки способности имплантата сохранять физиологическую функцию при использовании в системе кровообращения, для определения реакции организма-хозяина и реакции устройства (физическая целостность, тканевая инкапсуляция при умерщвлении) и для оценки деградации имплантата</p> | <p>После имплантации двух закрывающих элементов в одну и ту же бедренную артерию их имплантировали на расстоянии &gt; 30 мм</p> | <p>значительных признаков местной непереносимости или образования тромба. Макроскопическое наблюдение не выявило никакой разницы между овцами или свиньей после имплантации закрывающих элементов в бедренные артерии. При макроскопическом исследовании не наблюдалось значительных признаков местной непереносимости или образования тромба. Макроскопическое наблюдение не выявило никакой разницы между овцами или свиньей после имплантации закрывающих элементов в бедренные артерии.</p> <p>Гистопатологический анализ места имплантации на овцах не выявил локальных неблагоприятных реакций. Внутренние и наружные диски имели признаки разрушения и в некоторых случаях были разбиты на более мелкие части. Внутренние диски были полностью интегрированы в неоинтимальную ткань. В ходе гистопатологического анализа на свинье наблюдались несколько больше воспалительных признаков вокруг внутренних и наружных дисков. У обоих животных многоволоконная нить</p> |
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|                                                                                                                                                                                                              |                                   |                                                        |                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                    | <p>проявляла несколько больше воспалительных признаков, чем материал диска, что является нормальным для плетеных шовных нитей из-за большей площади поверхности.</p> <p>Пройодимость сосуда измеряли через 5 недель с использованием трех различных способов: гистоморфометрического, гистоморфометрического в сочетании с измерением диаметра сосуда с помощью калибра и с помощью цветовой ультразвуковой доплерографии. Средняя проходимость сосудов у овец составляла от 60 до 80 % в зависимости от способа (12 наблюдений). Средняя проходимость сосуда у свиньи составляла от 40 до 80 % (2 наблюдения).</p> |
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| Первое клиническое исследование на людях                                                                                                                                                                     |                                   |                                                        |                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Название исследования                                                                                                                                                                                        | Год / доверительный интервал (CI) | Тип исследования                                       | Цели                                                                                                                                                                                                                                      | Основные этапы                                                                                                                                                                                                                                     | Потенциальные критерии приемлемости                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB      | Открытое, несравнительное, многоцентровое исследование | Целями исследования были определение безопасности, эффективности и производительности системы FemoSeal Vascular Closure System (системы FemoSeal) в целом и, в частности, закрывающих элементов, у пациентов, проходящих кардиологическую | <p>Исследование состояло из 2 частей</p> <p>Всего n = 80</p> <p>Часть 1 n = 20</p> <p>Часть 2 n = 60</p> <p>Показания к применению: Часть 1 – диагностическая катетеризация сердца с использованием бедренной артерии в качестве места доступа</p> | <p>Результаты гемостаза достигается с помощью устройства FS без сжатия</p> <p>- Часть 1 20/20 (100 %)</p> <p>- Часть 2 58/60 (97 %)</p> <p>Медианное время до гемостаза во время процедуры (часть 2) – 1,0 минута (мгновенный диапазон – 8 минут)</p>                                                                                                                                                                                                                                                                                                                                                               |

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|  |  |  | диагностику или интервенционные кардиологические процедуры с использованием доступа к бедренной артерии. | <p>Часть 2 – пациенты, проходящие диагностические и интервенционные кардиологические процедуры с использованием бедренной артерии в качестве места доступа</p> <p>30-дневный контроль</p> | <p><u>Время до восстановления способности передвигаться (в минутах)</u></p> <p>Часть 1.</p> <p>Медиана: 33,0</p> <p>среднее: 67,8</p> <p>Часть 2.</p> <p>медиана: 45</p> <p>среднее: 87,5</p> <p><u>Частота серьезных сосудистых осложнений – контроль через 30 дней</u></p> <p>Часть 1</p> <p>-Без сосудистых осложнений 20/20 (100 %)</p> <p>Часть 2</p> <p>Псевдоаневризма – 1/59 (1,69 %)</p> <p><u>Ошибка лечения</u></p> <p>Часть 1 – 0/20 (0 %)</p> <p>Часть 2 – 3/60 (5 %)</p> <ul style="list-style-type: none"> <li>2 из-за невозможности достижения гемостаза без сжатия</li> <li>1 из-за серьезного сосудистого осложнения, псевдоаневризма</li> </ul> <p><u>Постоянное выделение</u></p> <p>Часть 1 – 0/20 (0 %)</p> <p>Часть 2- 8/60 (13 %)</p> <p><u>Гематома</u></p> <p>Часть 1 – 0/20 (0 %)</p> <p>Часть 2 – 6/60 (10 %)</p> |
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В рамках плана разработки FemoSeal™ VCS до выхода на рынок были проведены три функциональных теста на животных. В 2000 году, до начала клинических исследований, было проведено исследование на животных для оценки биофункциональности системы FemoSeal™ VCS. В данном исследовании оценивалась способность закрывающих элементов сохранять физиологическую функцию и определялась степень их деградации. Через 18 месяцев материал внутреннего и наружного дисков больше не был виден, его заменила эндолумбальная фиброзная ткань. В заключение было подтверждено способность закрывающего элемента FemoSeal™ VCS сохранять физиологическую функцию при использовании в системе кровообращения.

В 2002 году было проведено исследование на животных для оценки биосовместимости и биофункциональной возможности биоразлагаемого имплантата FemoSeal™ VCS, предназначенного для достижения гемостаза в сосудистой системе. Таким образом, разложение имплантата было почти завершено к 36 неделям, и существенных неблагоприятных тканевых реакций не наблюдалось.

В другом исследовании на животных, проведенном в 2002 году, оценивались биосовместимость и биофункциональность биоразлагаемого имплантата FemoSeal™ VCS, предназначенного для достижения гемостаза в сосудистой системе. Через 5 недель инкапсуляция диска была завершена, и наблюдались признаки разложения внутренних и внешних дисков. В заключение была подтверждена способность имплантата поддерживать физиологическую функцию при использовании в системе кровообращения.

В рамках плана клинических разработок системы FemoSeal™ VCS компания Radi Medical System AB провела предпродажное маркетинговое клиническое исследование. Данное клиническое исследование не опубликовано и недоступно в Интернете. Исследование с использованием устройства модели #11200 было проведено в 2002-2004 гг. в соответствии с европейским стандартом EN 540 (Клинические исследования медицинских устройств на людях) и в соответствии с Общими положениями ICH по клиническим испытаниям и Руководством по надлежащей клинической практике. Подробные сведения об этом исследовании приведены в отчете EU-SE-001. Клиническое исследование было задокументировано в итоговом отчете компании Radi Medical Systems AB «Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures». Клиническое исследование было проведено с использованием FemoSeal™ первой модели #11200 и было посвящено безопасности и действенности имплантируемых закрывающих компонентов.

Единственное различие между первой моделью #11200 и текущей моделью, C11202, заключается в размере по французской шкале, 6F и 7F соответственно, и улучшенной системе доставки. Клинические преимущества, целевое использование, принципы работы и исходные материалы имплантируемых закрывающих элементов, внутреннего уплотнителя и внешнего закрывающего диска остаются неизменными.

Устройство предназначалось для пациентов, проходящих диагностические кардиологические или интервенционные процедуры с использованием бедренной артерии в качестве точки доступа. Целью данного исследования было определение безопасности, производительности и эффективности системы FemoSeal™ VCS. Это было перспективное, многоцентровое, несравнительное открытое исследование с 30-дневным контролем.

Первичной конечной точкой оценки эффективности было время до гемостаза, определяемое как отсутствие острого кровотечения. Первичной конечной точкой безопасности была частота серьезных сосудистых осложнений в течение 30 дней. Вторичные конечные точки включали время до восстановления способности передвигаться, долю неудачного лечения, частоту нежелательных явлений и характеристики устройства во время доставки и размещения.

Пациенты, включенные в данное исследование, были взрослыми, способными дать информированное согласие и с пульсом хотя бы в одной неосложненной нижней конечности. Пациенты были исключены из исследования при наличии любого из следующих состояний:

- Заболевания периферических сосудов в анамнезе
- Аутоиммунные заболевания
- Известное нарушение кровотечения при тяжелой анемии
- INR >1,5
- Инфаркт миокарда в течение 72 часов
- Неконтролируемая гипертония, несмотря на лечение
- Ожирение, исключающее доступ с помощью техники Сельдингера
- Наличие сосудистого имплантата или стента в месте артериотомии
- Предыдущая ипсилатеральная пункция в течение 3 месяцев
- Ожидаемая продолжительность жизни < 6 месяцев

Кроме того, пациенты исследовались во время операции и исключались из исследования при наличии любого из следующих признаков:

- Диаметр просвета общей бедренной артерии <5 мм
- Артериальные ветви в пределах 2 см проксимальнее места пункции
- Сильный стеноз в пределах 3 см от места пункции
- Использование первичного интродьюсера >6Fr
- Пункция в области бифуркации бедра или дистальнее нее

- Многократные пункции бедра
- Известная или подозреваемая пункция задней стенки бедренной артерии
- Большая гематома (2:6 см) после завершения процедуры
- Сложное введение первичного интродьюсера для процедуры из-за извилистой ткани или сосуда

Данное исследование с использованием одного протокола проводилось в двух частях: В первую часть было включено 20 пациентов, затем был проведен анализ безопасности, а во вторую часть было включено еще 60 пациентов.

В части 1 средний возраст зарегистрированных пациентов составил 65,9 года, 70,0 % пациентов были мужчинами, а 95 % пациентов принимали сопутствующие лекарства. Во второй части исследования средний возраст составлял 63,8 года, 78 % были мужчинами, а 100 % принимали сопутствующие лекарства.

Пациенты, которым проводили диагностические (часть 1 и часть 2) или интервенционные (часть 2) процедуры катетеризации сердца, имели право на участие в исследовании.

Процедуры соответствовали стандарту ухода в каждой из регистрирующих больниц с последующим использованием системы FemoSeal™ VCS. Данные о пациенте собирали на исходном уровне, во время процедуры и через 1 день и 30 дней после процедуры.

Результаты представлены в **таблице 1.5** и указывают на то, что система FemoSeal™ VCS безопасна и эффективна для использования в данной популяции пациентов.

**Таблица 1.5. Клинические результаты, представленные в предпродажном исследовании**

|                                                                                                                       | <b>Часть 1</b> | <b>Часть 2</b>           |
|-----------------------------------------------------------------------------------------------------------------------|----------------|--------------------------|
| Число пациентов                                                                                                       | 20             | 60                       |
| Среднее время до гемостаза                                                                                            | 1,2 минуты     | 1,6 минуты <sup>a</sup>  |
| Среднее время до восстановления способности передвигаться                                                             | 72,2 минуты    | 87,5 минуты <sup>b</sup> |
| Распространенность основных сосудистых осложнений <sup>c</sup>                                                        | 0 (0 %)        | 1 (2 %)                  |
| Число пациентов с нежелательными явлениями                                                                            | 5 (25 %)       | 19 (32 %)                |
| Неудачное лечение (определяется как серьезные сосудистые осложнения, необходимость ручного сжатия или и то, и другое) | 0 (0 %)        | 3 (5 %)                  |
| Неисправности устройства                                                                                              | 0 (0 %)        | 6 (10 %)                 |

<sup>a</sup> На основании общего размера выборки 58, поскольку 2 больных не достигли гемостаза во время процедуры из-за предыдущих ипсилатеральных пункций. Гемостаз был достигнут через 7 минут и 37 минут для этих пациентов.

<sup>b</sup> На основании общего размера выборки 59: один пациент не был включен в исследование, поскольку его поместили на аппарат ИВЛ из-за отека легких и не мог передвигаться более недели.

<sup>c</sup> Определяется как сосудистое осложнение, требующее переливания крови или хирургического восстановления, или местное инфицирование, требующее введения антибиотика, госпитализации или продления госпитализации, или санации участка

В части 1 исследования не наблюдалось серьезных сосудистых осложнений. В части 2 исследования отмечено одно серьезное сосудистое осложнение: псевдоаневризма, о которой сообщалось в течение одного дня после процедуры. В результате потребовались сжатие под ультразвуковым контролем и инъекция тромбина в псевдоаневризму, а также продление госпитализации пациента.

Из пяти нежелательных явлений, отмеченных в части 1 исследования, было одно, возможно, связанное с устройством нежелательное явление: несерьезное событие, связанное с острым кровотечением, через 1 день после процедуры. Из 19 нежелательных

явлений, отмеченных в части 2 исследования, были отмечены три связанных с устройством несерьезных нежелательных явления гематомы, а также шесть возможных несерьезных явлений, связанных с устройством, включая три сообщения о постоянном просачивании, две гематомы и один случай боли в ногах после упражнения.

В части 2 три пациента считались получившими неудачное лечение: двое из-за неудачного достижения гемостаза без применения сжатия и один — из-за серьезного сосудистого осложнения (псевдоаневризмы). В части 1 исследования не было случаев неудачного лечения.

Из шести неполадок устройства, выявленных в части 2 исследования, три не препятствовали проведению процедуры. Одна из них была вызвана ошибкой пользователя, одна – протечкой интродьюсера, а другая – поломкой сочленения многоволоконной нити. Последние две проблемы были решены с помощью обновлений модели, реализованных в C11202.

Часть 2 предпродажного клинического исследования не сообщала о результатах последующего контроля через 6 месяцев из-за несоблюдения пациентом требований. Результаты предпродажного клинического исследования (EU-SE-001) за 30 дней, которые соответствуют срокам наблюдения в клинической литературе, свидетельствуют о безопасности и эффективности системы FemoSeal™ VCS.

### 1.4.2 Сводные данные послепродажных клинических исследований

В **таблице 1.6** ниже приведены четыре завершенных послепродажных клинических исследования. Эти клинические исследования не опубликованы и недоступны в Интернете.

**Таблица 1.6. Послепродажные клинические исследования**

| Завершенные послепродажные клинические исследования                                         |                                   |                                                                            |                                                                                                                                                                                                                                     |                                                                                                                                                                                                         |                                                                                                                                                       |
|---------------------------------------------------------------------------------------------|-----------------------------------|----------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|
| Название исследования                                                                       | Год / доверительный интервал (CI) | Тип исследования                                                           | Цели                                                                                                                                                                                                                                | Основные этапы                                                                                                                                                                                          | Потенциальные критерии приемлемости                                                                                                                   |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br><br>RADI                  | Послепродажное исследование: приемлемость для пользователей новой упаковки | Послепродажное исследование проведено на обновленной системе FemoSeal Vascular® Closure System #11202, которая имеет модифицированную систему доставки по сравнению с первой моделью #11200, для документирования функциональности. | 100 пациентов <ul style="list-style-type: none"> <li>63 мужчины / 37 женщин</li> <li>Средний возраст 68 лет для женщин, 65 лет для мужчин</li> </ul> 2 шведские больницы, 6 врачей<br><br>112 устройств | Результаты<br><br>1. Иллюстрации/указания в инструкции по эксплуатации считаются информативными и адекватными.<br><br>2. Мгновенный гемостаз (91/100) |

|                                                                                   |                                                                                  |                                      |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
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|                                                                                   |                                                                                  |                                      | Цель исследования заключалась в том, чтобы получить обратную связь по обновленной Инструкции по применению (IFU), учебному проекту для врачей и медсестер, подтвердить оценки, сделанные при анализе рисков, и внести свой вклад в улучшение качества продукции.                  | Данные, собранные в формах истории болезни пациента (CRF)<br><br>Планируемое время наблюдения – 30 минут с момента применения                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008) | Доктор Николас Моес (Nicolas Moes), Медицинский университет г. Инсбрука, Австрия | Послепродажная подтверждающая оценка | Целью данного исследования была оценка безопасности и эффективности FemoSeal®, используемого в ходе обычного клинического лечения у пациентов, проходящих диагностическую катетеризацию сердца или чрескожную интервенционную процедуру на сердце, проводимую с 7F-интродьюсером. | 50 последовательных пациентов<br><br>Показания – диагностическая или инвазивная катетеризация сердца из общей бедренной артерии<br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.6±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.6±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Основные конечные точки <ul style="list-style-type: none"><li>Первичная конечная точка эффективности — ТТН (время до гемостаза) с выделениями или без выделений, но без дополнительного сжатия, ручного или механического.</li><li>Конечная точка безопасности – частота нежелательных явлений – мелких и серьезных сосудистых осложнений и всех других нежелательных явлений – серьезных и несерьезных во время исследования (т. е. до выписки пациента).</li></ul> Результаты <ul style="list-style-type: none"><li>Среднее время до гемостаза</li><li>Диагностическая катетеризация – 56,6 ± 29 секунд</li><li>Интервенционная процедура – 59,9 ± 16,2 секунды</li><li>Все пациенты 57,8 ± 26,3</li><li>После 4-часового постельного режима пациенты могут без проблем передвигаться.</li></ul> Безопасность <ul style="list-style-type: none"><li>49/50 (98 %) без сосудистых осложнений до выписки из больницы</li></ul> |
| n                                                                                 | 50                                                                               |                                      |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| men                                                                               | 35 (70%)                                                                         |                                      |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| women                                                                             | 15 (30%)                                                                         |                                      |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| PCI cases                                                                         | 15                                                                               |                                      |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| age (yrs)                                                                         | 62.6±11.1                                                                        |                                      |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| body mass index (kg/m²)                                                           | 25.4±6.7                                                                         |                                      |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| systolic BP (mmHg)                                                                | 131.2±20.9                                                                       |                                      |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| diastolic BP (mmHg)                                                               | 77.9±10.6                                                                        |                                      |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| diabetes mellitus                                                                 | 9 (18%)                                                                          |                                      |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| arterial hypertension                                                             | 34 (68%)                                                                         |                                      |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| previous coronary intervention                                                    | 13 (26%)                                                                         |                                      |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| preprocedure aspirin                                                              | 50 (100%)                                                                        |                                      |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| preprocedure clopidogrel                                                          | 50 (100%)                                                                        |                                      |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Procedural unfractionated heparin                                                 | 15 (30%)                                                                         |                                      |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Procedural abciximab                                                              | 2 (4%)                                                                           |                                      |                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |   |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |



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|                                                                                                                                 |                                 |                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                         | <ul style="list-style-type: none"> <li>Среднее время до выписки 2,6 дня</li> <li>1/50 (2 %) незначительное кровотечение на следующий день после восстановления способности передвигаться без происшествий в день ангиографии</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | 2009 RADI                       | Послепродажное исследование                                                | <p>Исследование должно информировать клиентов/пользователей о любых проблемах с новой упаковкой, особенно о нестерильной наружной стороне пакета Tuvek/ПЭТ-ПЭ.</p> <p>В исследовании также должна быть представлена информация о том, видит ли лечащий врач какие-либо различия в этапах применения/размещения устройства по сравнению с ранее использованными устройствами.</p> <p>Кроме того, исследование должно выявить дополнительные потребности в улучшении качества продукции.</p> | <p>25 устройств</p> <p>4 шведские больницы</p> <p>16/25 (64 %) пациентов были пациентами с ЧКВ с сильными антикоагулянтами</p>                                                                                                                                                                                                                          | <p>Результаты</p> <ol style="list-style-type: none"> <li>Проблемы, связанные с упаковкой – 21/25 (84 %) случаев применения были успешными; 4/25 (16 %) случаев были неудачными (1 – тестирование нового интродьюсера, 1 внутренний диск прошел через артериотомию на этапе поддержки, кнопка поднялась и внешний диск был помещен в разрез в тканевом канале, 2 мгновенный гемостаз не был достигнут, несмотря на отсутствие проблем с установкой системы).</li> <li>Мгновенный гемостаз 19/25 (76 %) пациентов</li> <li>Кровотечение 11/25 (44 %) – 9/25 (36 %) выделения/кровотечения, 2/25 (8 %) гематомы</li> </ol> <p>Общая частота событий 19 %</p> |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022) | 2022/Terumo Medical Corporation | Перспективное, многоцентровое, наблюдательное, послепродажное исследование | Целью данного исследования является дальнейшая демонстрация безопасности и эффективности системы FemoSeal™ VCS при достижении гемостаза в месте доступа к общей бедренной артерии (CFA) у реальных субъектов, проходящих чрескожные эндоваскулярные процедуры.                                                                                                                                                                                                                             | <ul style="list-style-type: none"> <li>Контроль пациента через 30 дней (<math>\pm</math> 7 дней) посредством визита в больницу или телефонного звонка.</li> <li>Регистрация: с декабря 2021 г. по июль 2022 г.</li> <li>Используются 230 включенных в исследование субъектов, проходящих диагностические или интервенционные эндоваскулярные</li> </ul> | <ul style="list-style-type: none"> <li><b>Демография/сопутствующие заболевания:</b> <ul style="list-style-type: none"> <li>Пол: 161 мужчина (70 %)/69 женщин 69 (30 %).</li> <li>Средний возраст: 70 <math>\pm</math> 12.</li> <li>ИМТ: 26,1 <math>\pm</math> 4,95 кг/м<sup>2</sup>.</li> <li>Гипертензия: 160 пациентов (69,6 %).</li> <li>Дислипидемия: 128 (55,7 %).</li> </ul> </li> </ul>                                                                                                                                                                                                                                                            |

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|  |  |  |  | <p>процедуры, в которых используется устройство FemoSeal™.</p> <p>3 места проведения исследований в Европе: Франция (92 пациента), Германия (38 пациентов), Бельгия (100 пациентов).</p> | <ul style="list-style-type: none"> <li>- Коронарная недостаточность: 42 (18,3 %).</li> <li>- Курящий в настоящее время: 86 (37,6 %).</li> <li>- Ранее курил: 66 (28,8 %).</li> <li>- Ишемическая болезнь сердца: 34 (14 %).</li> <li>- Ранее перенесенный инфаркт миокарда: 18 (7,8 %).</li> <li>- Реваскуляризация периферической артерии: 12 (5,2 %) сонная артерия и 83 (37,5 %) и артерия нижней конечности.</li> <li>- Антитромбоцитарная терапия (на исходном уровне): 211 (91,7 %), включая 21 (9,1 %) двойную антитромбоцитарную терапию (ДАТТ).</li> <li>- Пероральная антикоагуляция: 40 (17,4 %) пациентов.</li> <li>• <b>Характеристики вмешательства:</b> <ul style="list-style-type: none"> <li>- Условия: стационарная клиника 162 случая (70,4 %), амбулаторная клиника 68 случаев (29,6 %).</li> <li>- Преобладающее показание: клаудикация 147 случаев (63,9 %).</li> <li>- Порядок действий: 35 антеградных (15,3 %), 194 ретроградных (84,7 %).</li> </ul> </li> <li>• <b>Основные конечные точки:</b> <ul style="list-style-type: none"> <li>- Комбинированная конечная точка безопасности (отсутствие серьезных осложнений в конечности в месте доступа в течение 6 часов после процедуры)</li> </ul> </li> </ul> |
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|  |  |  |  |  | <div>и эффективности (успешный гемостаз в месте пункции) достигнута в 215/226 (95,1 %) [95 % ДИ: 91,46; 97,55] пациентов в полном наборе для анализа и 215/230 (93,5 %) [95 % ДИ 89,47, 96,30] в обработанном наборе FemoSeal™.</div> <div>- Конечная точка эффективности была достигнута у 219/226 (96,9 %) пациентов с ДИ [93,7, 98,7].</div> <div>- Конечная точка безопасности достигнута в 220/230 (95,2 %) [95 % ДИ: 92,15, 97,90] пациентов.</div> <div> <div>• Вторичные конечные точки:</div> <div>- Отсутствие незначительных осложнений в месте доступа в течение шести часов после процедуры достигнуто у 225/230 (97,8 %) [95 % ДИ: 95,00; 99,29].</div> <div>- Отсутствие серьезных и незначительных осложнений в месте доступа с шести часов до 30 дней после процедуры было достигнуто у 219/230 (95,2 %) пациентов [95 % ДИ: 91,60; 97,59].</div> <div>- Медианное время до гемостаза при использовании FemoSeal™ VCD: 0,42 (0,25; 0,50) минуты.</div> <div>- Среднее время до восстановления способности передвигаться: 5,00 (4,54; 5,50) минут.</div> </div> |
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|  |  |  |  |  | <p>- Средняя продолжительность пребывания в больнице: 23,98 (22,72, 25,00) часов.</p> <p>- Удобство использования системы FemoSeal™ VCS: «просто» или «очень легко» устанавливать в 98,7 % случаев («просто» устанавливать в 21 (9,2 %), «очень легко» устанавливать в 205 (89,5 %) случаев) с отсутствием или низким сопротивлением при установке в 226 (98,3 %) случаев.</p> <p>152/230 (66,1 %) пациентов, прошедших лечение с использованием проводника, входящего в комплект FemoSeal™ (проводник 0,038 дюйма), и рекомендованного в FemoSeal™, без каких-либо зарегистрированных дефектов устройства или нежелательных явлений.</p> |
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Исследование 2006 года было проведено для подтверждения безопасности и эффективности текущего устройства с усовершенствованной системой доставки и для получения обратной связи по инструкции по применению FemoSeal™ VCS и учебной программе. Исследование включало 100 пациентов, и основной конечной точкой было достижение гемостаза или необходимость дополнительного ручного или механического сжатия. В ходе данного исследования было сделано заключение о том, что применение системы VCS FemoSeal™ было успешным в большинстве случаев (91 % достигли мгновенного гемостаза).

В исследовании 2008 года приняли участие 50 пациентов для оценки безопасности и эффективности системы VCS FemoSeal™ при ее использовании во время обычных клинических процедур у пациентов, которым проводилась катетеризация сердца с использованием интродьюсера калибра 7 Fr. Основной конечной точкой исследования был сбор данных о времени до гемостаза и времени до восстановления передвижения без дополнительного сжатия, ручного или механического. Результаты исследования показали,

что среднее время до достижения гемостаза составило 57,8 секунды, и все пациенты ходили после 4 часов постельного режима.

Исследование 2009 года было посвящено оценке новой упаковки FemoSeal™ VCS. В исследовании приняли участие 25 пациентов. Первичной конечной точкой было то, испытывал ли пользователь какие-либо проблемы с упаковкой. Пользователи не замечали никаких проблем с новой упаковкой FemoSeal™ VCS. В ходе этого исследования также собирались данные о времени до гемостаза.

Целью исследования 2022 г. был проактивный сбор данных о безопасности и эффективности FemoSeal VCS при достижении гемостаза в месте доступа к общей бедренной артерии (CFA) у реальных пациентов, проходящих чрескожные эндоваскулярные процедуры. В исследовании приняли участие 230 пациентов. Основными конечными точками для регистрации являются успешное выполнение процедуры (т. е. удачный гемостаз в месте пункции) и уменьшение серьезных осложнений (например, повреждение сосудов, кровотечение, связанное с местом доступа, инфицирование места доступа, повторное ручное сжатие и ипсилатеральная острая ишемия ног, связанная с новым местом доступа). Исследование показало, что система FemoSeal™ VCS хорошо работает в реальных условиях и обеспечивает эффективный гемостаз и низкий уровень осложнений в месте доступа у пациентов, проходящих периферические эндоваскулярные вмешательства. Он демонстрирует хорошие эксплуатационные характеристики с коротким временем до гемостаза и хорошими отзывами операторов о практической применимости, что делает FemoSeal VCS ценным устройством для закрытия бедренного доступа.

### **1.4.3 Сводные данные послепродажного клинического контроля**

#### **1.4.3.1 Завершенный послепродажный клинический контроль**

Сводная информация о выполненных мероприятиях по послепродажному клиническому контролю приведена в **таблице 1.7** ниже.

**Таблица 1.7. Послепродажный клинический контроль**

| Завершенные мероприятия по послепродажному клиническому контролю          |                                   |                                                                    |                                                                                                                                                                                                     |                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
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| Название мероприятия                                                      | Год / доверительный интервал (CI) | Тип исследования                                                   | Цели                                                                                                                                                                                                | Основные этапы                                                                                                                                                                                      | Потенциальные критерии приемлемости                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021 TMC                          | Послепродажный клинический опрос — высококачественное исследование | Послепродажное исследование для сбора ожидаемых отзывов в связи с использованием устройства для закрытия сосудов FemoSeal™ Vascular Closure Device, распространяемого на рынках Европейского союза. | <ul style="list-style-type: none"> <li>120 случаев</li> <li>8 уникальных врачей, имеющих более 5 лет опыта</li> <li>Многие страны Европы</li> </ul>                                                 | <b>Оценки устройств по шкале 1-5 — утверждения опроса</b> <ul style="list-style-type: none"> <li>Критерии приемлемости <ul style="list-style-type: none"> <li>Оценки 3-5 считаются благоприятными</li> <li>Все утверждения должны содержать <math>\geq 80\%</math> положительных отзывов</li> </ul> </li> <li>Результаты <ul style="list-style-type: none"> <li>Ни одно из утверждений опроса не получило <math>&gt; 20\%</math> неблагоприятных ответов</li> <li>Жалоб на изделие не поступало</li> </ul> </li> </ul> |
| 20210298 – 0.035” and 0038” Guidewire Clinical Survey Report (2021)       | 2021 TMC                          | Послепродажный клинический опрос — высококачественное исследование | Послепродажное исследование для сбора ожидаемых отзывов в связи с использованием проводника                                                                                                         | <ul style="list-style-type: none"> <li>Опросы для проводника 0,035 <ul style="list-style-type: none"> <li>106 опросов</li> <li>64 врача</li> </ul> </li> <li>Опросы для проводника 0,038</li> </ul> | <b>Оценки устройств по шкале 1-5 — утверждения опроса</b> <ul style="list-style-type: none"> <li>Критерии приемлемости <ul style="list-style-type: none"> <li>Оценки 3-5 считаются благоприятными</li> </ul> </li> </ul>                                                                                                                                                                                                                                                                                               |

| Завершенные мероприятия по послепродажному клиническому контролю                                                                |                  |                                                                    |                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                            |
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|                                                                                                                                 |                  |                                                                    | размером 0,035 дюйма, входящего в состав устройства для закрытия сосудов Angio-Seal™ VIP Vascular Closure Device (VCD) размером 6 Fr, и проводника размером 0,038 дюйма, входящего в состав устройств Angio-Seal™ VIP VCD размером 8 Fr и FemoSeal Vascular Closure System, продаваемых на рынках Европейского союза. | <ul style="list-style-type: none"> <li>○ 109 опросов</li> <li>○ 55 врачей</li> <li>• 12 ретроспективных опросов</li> </ul>                                                                                                                                                                            | <ul style="list-style-type: none"> <li>○ Все утверждения должны содержать ≥ 80 % положительных отзывов</li> <li>• Результаты <ul style="list-style-type: none"> <li>○ Все проводники получили приемлемые оценки</li> <li>○ Жалоб на изделие не поступало</li> </ul> </li> </ul>                                            |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023—2024 TMC/TE | Послепродажный клинический опрос — высококачественное исследование | Перспективный сбор отзывов, связанных с использованием FemoSeal VCS с проводниками, распространяемыми на рынке ЕС.                                                                                                                                                                                                    | <ul style="list-style-type: none"> <li>• 126 опросов</li> <li>• 7 объектов</li> <li>• 5 стран</li> <li>• 14 ноября 2023 г. — 11 июня 2024 г.</li> <li>• Медицинский специалист: <ul style="list-style-type: none"> <li>○ сосудистый хирург</li> <li>○ интервенционный радиолог</li> </ul> </li> </ul> | <b>Оценки устройств по шкале 5 — утверждения опроса</b> <ul style="list-style-type: none"> <li>• Критерии приемлемости <ul style="list-style-type: none"> <li>○ Оценки 3-5 считаются благоприятными</li> <li>○ Все утверждения должны содержать ≥ 80 % положительных отзывов</li> <li>○ Если в ходе</li> </ul> </li> </ul> |

| Завершенные мероприятия по послепродажному клиническому контролю |  |  |  |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
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|                                                                  |  |  |  | <div>○ ангиолог</div> | <div>данного опроса возникают нежелательные явления, они должны соответствовать ожидаемым в рамках управления рисками.</div> <div> <ul style="list-style-type: none"> <li>Демографические данные пациентов <ul style="list-style-type: none"> <li>женщины: 29,4 % (37/126)</li> <li>мужчины: 69,8 % (88/126)</li> <li>Пол не указан: 0,8 % (1/126)</li> <li>Возраст 75 лет и более: 31,7 %</li> </ul> </li> <li>Результаты <ul style="list-style-type: none"> <li>Проводник, поставляемый с FemoSeal™ VCS: 101/126 (80,2 %).</li> <li>Максимальная продолжительность процедуры (в минутах) 63,4 (36,6)</li> </ul> </li> </ul> </div> |



| Завершенные мероприятия по послепродажному клиническому контролю |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
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|                                                                  |  |  |  |  | <div> <div> (среднее (SD));<br/> 57,0<br/> (36,0—81,0)<br/> (среднее (IQR)) </div> <div> <div>○ Все оценки эффективности FemoSeal™ VCS были благоприятными.</div> <div>○ Все оценки проводника, поставляемого с системой FemoSeal™ VCS, были благоприятными.</div> <div>○ Одно нежелательное явление (0,8 %): диски FemoSeal™ VCS были неправильно выровнены, вероятно, из-за использования жесткого проводника (Boston Scientific Amplatz Super Stiff, 75 см, 0,035 дюйма), что требовало ручного сжатия для достижения гемостаза.</div> </div> </div> |

В течение текущего отчетного периода (01 сентября 2019 г. - 31 августа 2024 г.) компания Terumo Medical Corporation провела три высококачественных опроса врачей-пользователей.

В ходе клинических исследований FemoSeal™ были собраны проактивные клинические данные о безопасности и эффективности системы FemoSeal™ VCS во время клинического использования. Опрос включал вопросы, касающиеся всего устройства и сопутствующих принадлежностей, включая проводник 0,038 дюйма, а также их непосредственного взаимодействия. В ходе клинических исследований с использованием проводника диаметром 0,038 дюйма, поставляемого с системой FemoSeal™ VCS, были собраны проактивные клинические данные, связанные с безопасностью и эффективностью использования проводника. В ходе опроса основное внимание уделялось общему использованию проводника, начиная с введения через процедурный интродьюсер в сосудистую сеть и заканчивая извлечением проводника.

FemoSeal™ VCS и проводник 0,038 дюйма, входящие в комплект поставки устройства, получили приемлемые оценки; было подано 6 (шесть) жалоб на устройство и 9 (девять) претензий к проводнику на основании оценки комментариев, полученных в ходе высококачественных клинических исследований. Жалобы были оценены как для FemoSeal, так и для проводника, и рассмотрены в рамках процесса послепродажного наблюдения Terumo. Новые риски и/или уровни риска не определены.

Опрос врачей-пользователей был проведен в 2024 году в рамках мероприятий PMCF. Результаты опроса показали, что эффективность и безопасность системы FemoSeal™ VCS в целом оказались очень благоприятными. Также была продемонстрирована совместимость с проводниками, отличными от стандартных проводников, поставляемых с FemoSeal™ VCS.

#### **1.4.3.2 Текущий или запланированный послепродажный клинический контроль**

TMC один раз проводит текущий/планируемый послепродажный клинический контроль. Будет проведен клинический опрос с целью сбора обратной связи, связанной с использованием проводника с системой FemoSeal VCS распространяемой на рынке ЕС. Врачам предстоит заполнить анкету, чтобы узнать, какие проводники они использовали во время процедуры. Целью данного опроса является устранение пробела, выявленного как недостаток литературы и комментариев внешних экспертов по совместимости FemoSeal™ VCS с использованием проводников других производителей, не относящихся к компании Terumo. Обратная связь включает в себя технические результаты, клинические характеристики и безопасность, относящиеся к работе устройства с различными проводниками.

#### 1.4.4 Сводные данные из систематического обзора литературы

Компания Terumo Medical Corporation проводит систематические обзоры литературы для сбора и оценки клинических данных по безопасности и эффективности, полученных в ходе опубликованных исследований устройства FemoSeal™ VCS и/или аналогичных устройств. Цель ежегодного анализа опубликованной литературы заключается в выявлении ранее неизвестных побочных эффектов, отслеживании известных побочных эффектов, определение возникающих рисков, а также выявлении возможного систематического неправильного или не предусмотренного инструкцией использования устройства FemoSeal™ VCS.

В последнем систематическом обзоре литературы, охватывающем период с 1 сентября 2019 г. по 31 августа 2024 г., было выявлено 29 опубликованных исследований, в которых были получены данные о клинической безопасности и эксплуатационных характеристиках устройства FemoSeal™ VCS. В 23 исследованиях сообщалось о применении FemoSeal™ VCS по инструкции, а о применении не по инструкции сообщалось в девяти исследованиях. В целом, обзор литературы по исследованиям, характерным для использования FemoSeal™ VCS, показывает исследуемую популяцию, которая является репрезентативной для пациентов в ЕС, проходящих чрескожную сосудистую катетеризацию. Список 23 рецензируемых публикаций касательно исследований по одобренным показаниям с отзывами коллег см. в разделе 3.

Клинические показатели оценивались по следующим показателям:

- Время до гемостаза лучше или сопоставимо с уровнем современного состояния технологии чрескожного закрытия общей бедренной артерии.
- Время до восстановления способности передвигаться лучше или сравнимо с уровнем современного состояния технологии чрескожного закрытия общей бедренной артерии.
- Частота послеоперационных осложнений сопоставима или ниже, чем текущие стандарты лечения.

На основании этих клинических показателей данные, представленные в данной обзорной литературе, показали, что FemoSeal™ VCS можно успешно использовать для закрытия пункции бедренной артерии (артериотомии) у пациентов, которым проводилась чрескожная катетеризация с использованием процедурного интродьюсера размером 7 Fr или меньше. Полный гемостаз был достигнут у большинства пациентов (79,65-100 %) и был связан с медианой времени до гемостаза 0,5 мин, среднее время до выписки — 3 дня. От 69,2 до 86,7 % пациентов могли передвигаться через 5 часов после закрытия раны, со средним послеоперационным постельным режимом 349 минут. Неисправность системы FemoSeal™ VCS наблюдалась в 3,68-4 % случаев, а дополнительное ручное сжатие потребовалось в 0,9-4,4 % случаев.

Клиническая безопасность оценивалась по неблагоприятным явлениям, включая, помимо прочего, такие как:

- Кровотечение
- Гематома
- Псевдоаневризма
- Синяк
- Артериовенозная фистула
- Инфекция
- Летальный исход

Для каждого из этих нежелательных явлений частота возникновения, отмеченная для FemoSeal™ VCS во включенных исследованиях, была меньше или сопоставима с ранее зарегистрированной частотой для ручного сжатия и других устройств для закрытия сосудов.

В ходе изучения 10 отчетов о клинических случаях не было выявлено никаких нежелательных явлений, поскольку не было выявлено новых, непредвиденных, возникающих или неприемлемых рисков.

Общая эффективность использования FemoSeal™ VCS во время диагностической ангиографии или интервенционных операций зависит от множества факторов, таких как пол, возраст, анатомия пациента, сопутствующие заболевания, анатомическое расположение места пункции, опыт хирурга, метод размещения VCD, послеоперационный уход, и т. д. В дополнение к техническому успеху, включая достижение гемостаза, система FemoSeal™ VCS предлагала клинические преимущества по сравнению с закрытием сосудов после пункции бедренной артерии, такие как сокращение времени до гемостаза, сокращение времени до восстановления способности передвигаться. Фактические результаты для исследуемых устройств соответствуют ожидаемым для данного типа устройств при условии использования по назначению. Некоторые из ссылок, полученных в течение текущего периода поиска, показали использование исследуемого устройства в анатомическом месте, отличном от общей бедренной артерии, и для закрытия артериотомии > 7 Fr, что считается нарушением инструкции по применению.

В ходе обзора не были выявлены неизвестные побочные эффекты, возникающие риски или возможное систематическое неправильное использование устройства. Тем не менее, если FemoSeal™ VCS используется с осторожностью подготовленными врачами, это медицинское изделие является полезным и необходимым клиническим изделием. В целом целевая терапия и, следовательно, система FemoSeal™ VCS удовлетворяют клиническим потребностям, существующим в настоящее время в лечении осложнений, которые связаны с сосудистым доступом.

В целом, данные, приведенные в настоящей литературе, не выявили каких-либо проблем с эффективностью или безопасностью в клинических условиях, которые ранее были неизвестны, или неблагоприятных эффектов, которые имели место с более высокой ожидаемой/допустимой частотой. Таким образом, из этой литературы можно сделать вывод о том, что система VCS FemoSeal™ при использовании для обеспечения сжатия с целью гемостаза при артериотомии после чрескожной катетеризации продолжает работать в соответствии с ожиданиями и не связана с серьезными событиями, связанными с безопасностью.

#### **1.4.5 Сводные данные послепродажных наблюдений**

Действует проактивная система PMS. Ежемесячно проводится анализ всех претензий в соответствии с внутренними производственными процедурами. Данные по жалобам проанализированы в период с 1 сентября 2019 г. по 31 августа 2024 г. В целом было представлено 28 отчетов по контролю медицинских изделий (MDV) и 476 отчетов о жалобах клиентов, представленных производителю. Из 28 сообщений о MDV 27 были связаны с нежелательными явлениями, одно — с неисправностью устройства. В течение отчетного периода было зарегистрировано два смертельных случая, но ни один из зарегистрированных смертельных исходов не был связан с исследуемым устройством. Из 476 жалоб, направленных производителю, наиболее частыми причинами жалоб были затруднения при разворачивании (146 случаев, частота 0,0142 %). Режим отказа при событиях извлечения устройства является вторым наиболее частым с частотой 0,0126 % (130 событий).

Продажи системы FemoSeal Vascular Closure System превышают 1 030 136 по всему миру и 827 833 в Европейской экономической зоне. Расчетная частота жалоб на основе глобальных продаж составляет 0,046 %. Общая частота поступления претензий клиентов очень низкая. Новые риски, не включенные в инструкцию по эксплуатации и документацию по рискам, не выявлены.

Частота возникновения нежелательных побочных эффектов приведена в **таблице 1.2**. В ходе рассмотрения претензий не было обнаружено новых непредвиденных, возникающих или неприемлемых рисков. Значительного увеличения частоты или тяжести известных нежелательных побочных эффектов не наблюдалось.

#### **1.4.6 Общие сводные данные о клинической эффективности и безопасности**

Система FemoSeal™ VCS показана к применению при закрытии общей бедренной артериальной пункции (артериотомии) у пациентов, которым проводилась чрескожная катетеризация с использованием процедурного интродьюсера размером 7F (2,33 мм) или меньше. Данная клиническая оценка основана на всестороннем анализе имеющихся до- и послепродажных клинических данных и литературы, относящейся к назначению устройства FemoSeal™ VCS.

Был проведен всесторонний обзор опубликованной литературы за период с 1 сентября 2019 г. по 31 августа 2024 г. Совокупность доказательств включала 29 исследований системы FemoSeal™ VCS. Доказательства, представленные в ходе клинической оценки, позволяют сделать вывод о том, что исследуемое устройство безопасно и эффективно при использовании по назначению, а любые риски или нежелательные побочные эффекты, которые могут быть связаны с устройством в нормальных условиях использования, представляют собой приемлемые риски в сравнении с преимуществами для пациента. Фактические результаты для исследуемых устройств соответствуют ожидаемым для данного типа устройств при условии использования по назначению.

К возможным нежелательным побочным эффектам, связанным с использованием FemoSeal™ VCS, относятся нежелательные явления, о которых обычно сообщают при альтернативных способах закрытия артериотомии, например кровотечение и гематома. В целом, частота возникновения нежелательных явлений, о которых сообщалось при использовании FemoSeal™ VCS, аналогична частотам, о которых сообщалось при ручном сжатии и использовании аналогичных устройств для закрытия сосудов. В частности, частоты возникновения кровотечения и гематомы, зарегистрированные для FemoSeal™ VCS, ниже, чем для аналогичных устройств для закрытия сосудов. Каждое из зарегистрированных нежелательных явлений, как из опубликованной литературы, так и из послепродажного наблюдения, было ранее выявлено (см. **раздел 1.3**).

Имеющиеся данные о клинической безопасности и эксплуатационных характеристиках свидетельствуют о том, что использование устройства FemoSeal™ VCS дает пациенту преимущество, перевешивая возможные риски при его использовании в соответствии с инструкцией по применению.

Как указано в предыдущих разделах выше, данные, предоставленные для FemoSeal™ VIP VCD, демонстрируют согласованность между данными, относящимися к оцениваемому устройству (например, использование устройства, показатели безопасности, клинические характеристики и клинические преимущества), идентифицированными эквивалентными устройствами и данными, относящимися к аналогичным устройствам, перечисленным в разделе «Современное состояние вопроса».

Перекрестный анализ данных по безопасности не выявил каких-либо различий между:

- данными, упомянутыми в разделе «Современное состояние вопроса»
- данными, специфическими для оцениваемого устройства
- данными, указанными в файле (файлах) управления рисками
- данными, указанными в маркировке и/или IFU (т.е. рассматриваются остаточные риски, которые должны быть доведены до сведения пользователя).

Клиническая безопасность подтверждается низким уровнем осложнений, выявленных в опубликованной рецензируемой клинической литературе, клинических исследованиях, спонсируемых компанией, обзором послепродажных данных, а также отсутствием отзыва продукта с рынка. Не было выявлено каких-либо проблем с производительностью, в изученной литературе описано использование испытываемого устройства FemoSeal™ VCS в соответствии с заявленным производителем назначением.

### **1.5 Возможные диагностические и терапевтические альтернативы**

Ручное сжатие традиционно используется для достижения гемостаза в месте артериотомии после катетеризации сосудов. Ручное сжатие сопряжено с длительной иммобилизацией пациента (до 8 часов после процедуры) а также со значительным дискомфортом и длительным пребыванием в больнице. В недавнем систематическом обзоре было обнаружено, что медианное время достижения гемостаза с ручным сжатием составляло 20,8 минуты.

Альтернативы ручному сжатию включают внешние гемостатические устройства, которые прилагают механическое сжатие к месту артериотомии. Эти устройства не сокращают время до гемостаза или восстановления способности передвигаться, а снижают потребности в персонале, заменяя ручное сжатие механическим. Частота нежелательных явлений, связанных с использованием механического сжатия, аналогична таковой при ручном сжатии.

Устройства для закрытия сосудов, такие как FemoSeal™ VCS, предназначены для закрытия артериотомии. Они направлены на сокращение времени до гемостаза и обеспечение более ранней способности передвигаться. В недавнем систематическом обзоре, включающем 13 коммерчески доступных устройств, было обнаружено, что медианное время достижения гемостаза с помощью устройства для закрытия сосудов составляло 5,4 минуты.

Медианное время гемостаза для отдельных устройств для закрытия сосудов составляло от 1 минуты (FemoSeal™ VCS) до 14 минут; при этом для большинства устройств это время составляло от 4 до 10 минут.<sup>1</sup>

Обычно сообщаемые нежелательные явления, связанные с закрытием участка артериотомии, при ручном сжатии, использовании внешних гемостатических устройств или устройств для закрытия сосудов, включают гематому, кровотечение в месте доступа, псевдоаневризму, артериовенозную фистулу и инфекцию. Такой же систематический обзор (34 рандомизированных контролируемых исследования, 14 401 пациент) показал, что частота нежелательных явлений между ручным сжатием и использованием устройств для закрытия сосудов была одинаковой, за исключением того, что при закрытии сосудов с использованием устройств кровотечение, как правило, было немного выше.



*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Предлагаемый профиль пользователя и обучение

Предполагаемыми пользователями FemoSeal™ Vascular Closure System являются врачи, прошедшие обучение и имеющие квалификацию для выполнения артериального доступа и закрытия при эндоваскулярных процедурах с использованием общей бедренной артерии, и принявшие участие в программе обучения врачей Terumo Medical Corporation FemoSeal™.

## 1.7 Применимые гармонизированные и общие стандарты

| Ссылка на стандарт | Текущий год соответствия/ред. | Описание                                                                                                                                 |
|--------------------|-------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070          | 2014/AMD1:2018                | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070       | 2014/A1:2018                  | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance       | May 20, 2021                  | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052         | 2015                          | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213         | 2017                          | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503         | 2020                          | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182         | 2019                          | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |



| Ссылка на стандарт | Текущий год соответствия/ред. | Описание                                                                                                                                                                 |
|--------------------|-------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 13485       | 2016/A11:2021                 | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 13485          | 2016                          | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 14644-1        | 2015                          | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1     | 2015                          | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2        | 2015                          | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2     | 2015                          | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3        | 2019                          | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3     | 2019                          | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1        | 2003                          | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1     | 2003                          | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2        | 2003/TC1:2004                 | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |

| Ссылка на стандарт   | Текущий год соответствия/ред. | Описание                                                                                                                                      |
|----------------------|-------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 14698-2       | 2003/TC 1:2004                | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| USP <788>            | Н/Д                           | PARTICULATE MATTER IN INJECTIONS                                                                                                              |
| Фармакопея ЕС 2.9.19 | Н/Д                           | Particulate Contamination: Sub-Visible Particles                                                                                              |
| IEC 62366-1          | 2015                          | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN 62366-1           | 2015                          | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN ISO 14971         | 2019/A11:2021                 | Medical devices — Application of risk management to Medical devices                                                                           |
| ISO 14971            | 2019                          | Medical devices — Application of risk management to Medical devices                                                                           |
| ASTM F1980           | 2016                          | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                                           |
| EN ISO 10993-1       | 2020                          | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                    |
| ISO 10993-1          | 2018                          | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                    |
| EN ISO 10993-2       | 2006                          | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                                                |
| ISO 10993-2          | 2006                          | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                                                |
| EN ISO 10993-3       | 2014                          | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity                          |
| ISO 10993-3          | 2014                          | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity                          |

| Ссылка на стандарт | Текущий год соответствия/ред. | Описание                                                                                                       |
|--------------------|-------------------------------|----------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-4     | 2017                          | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood               |
| ISO 10993-4        | 2017                          | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood               |
| EN ISO 10993-5     | 2009                          | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                             |
| ISO 10993-5        | 2009                          | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                             |
| EN ISO 10993-6     | 2016                          | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                  |
| ISO 10993-6        | 2016                          | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                  |
| EN ISO 10993-10    | 2023                          | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                 |
| ISO 10993-10       | 2021                          | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                 |
| EN ISO 10993-11    | 2018                          | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                |
| EN ISO 10993-11    | 2017                          | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                |
| EN ISO 10993-12    | 2021                          | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                 |
| ISO 10993-12       | 2021                          | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                 |
| EN ISO 10993-17    | 2009                          | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances |
| ISO 10993-17       | 2002                          | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances |

| Ссылка на стандарт | Текущий год соответствия/ред. | Описание                                                                                                                                                                     |
|--------------------|-------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-18       | 2020/A1:2022                  | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-18    | 2020/A1:2022                  | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-23    | 2021                          | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23       | 2021                          | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382         | 2018                          | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756          | 2017                          | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>           | Н/Д                           | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>          | Н/Д                           | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72     | 2019                          | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135       | 2014/A1:2019                  | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135          | 2014/A1:2018                  | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |

| Ссылка на стандарт | Текущий год соответствия/ред. | Описание                                                                                                                                                        |
|--------------------|-------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-7     | 2008/A1:2022                  | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                       |
| EN ISO 10993-7     | 2008/A1:2019                  | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                               |
| EN 556-1           | 2024                          | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices |
| EN ISO 11737-1     | 2018/A1:2021                  | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11737-1        | 2018/A1:2021                  | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| EN ISO 11138-1     | 2017                          | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-1        | 2017                          | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| EN ISO 11138-2     | 2017                          | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 11138-2        | 2017                          | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| EN ISO 15223-1     | 2016                          | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| ISO 15223-1        | 2016                          | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| EN 1041            | 2008/A1:2013                  | Information supplied by the manufacturer of medical devices                                                                                                     |

| Ссылка на стандарт | Текущий год соответствия/ред. | Описание                                                                                                                                                                   |
|--------------------|-------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 11607-1     | 2020/A1:2023                  | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| ISO 11607-1        | 2019/A1:2023                  | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| EN ISO 11607-2     | 2020/A1:2023                  | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ISO 11607-2        | 2019/A1:2023                  | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169         | 2016                          | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M  | 2016                          | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825         | 2018                          | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096         | 2011 (R 2019)                 | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M      | 2015                          | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24       | 2021                          | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3        | 2020                          | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |
| MDCG 2020-8        | 2020                          | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                             |

| Ссылка на стандарт | Текущий год соответствия/ред. | Описание                                                                                                                                                                                                                                                      |
|--------------------|-------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-7        | 2020                          | Post-market clinical follow-up (PMCF) Plan Template<br>A guide for manufacturers and notified bodies                                                                                                                                                          |
| MDCG 2020-6        | 2020                          | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                                                                                                          |
| MDCG 2019-9 v1     | 2022                          | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                                                                                      |
| MDCG 2019-8 v2     | 2020                          | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15       | 2020                          | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11       | 2021                          | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19       | 2021                          | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4     | 2021                          | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2        | 2019                          | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1        | 2019                          | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7        | 2018                          | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6        | 2018                          | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device                                                                                                                                                                |

| Ссылка на стандарт     | Текущий год соответствия/ред. | Описание                                                                                                                                                                                      |
|------------------------|-------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                        |                               | Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                                                  |
| MDCG 2018-4            | 2018                          | MDCG 2018-4 Annex: UDI database<br>Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                               |
| MDCG 2018-3<br>v1      | 2020                          | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25           | 2021                          | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2.12-2<br>Rev 2 | 2012                          | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                        |



## 2.0 БИБЛИОГРАФИЯ

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### 3.0 ХРОНОЛОГИЯ РЕДАКЦИЙ ДОКУМЕНТА

| Номер версии сводной информации о безопасности и клинических характеристиках (SSCP) | Дата выпуска      | Описание изменения                                           | Изменение, утвержденное уполномоченным органом                                                                                                                                                                                                                                                                                                                                                                       |
|-------------------------------------------------------------------------------------|-------------------|--------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022                                                                        | 20 января 2023 г. | Первоначальный выпуск, после сертификации MDR CE             | <p><input checked="" type="checkbox"/> Да</p> <p>Язык валидации: English</p> <p><input type="checkbox"/> Нет (применимо только к имплантируемым устройствам класса IIa или некоторым устройствам IIb (MDR, статья 52 (4), 2-й параграф), для которых SSCP еще не утвержден уполномоченным органом)</p> <p><input type="checkbox"/> Другое (укажите):</p>                                                             |
| SSCP-FS-2023 – редакция 1                                                           | 15 марта 2024 г.  | Обновлено за период с 1 января 2019 г. по 31 декабря 2023 г. | <p><input checked="" type="checkbox"/> Да</p> <p>Язык валидации: English</p> <p><input type="checkbox"/> Нет (применимо только к имплантируемым устройствам класса IIa или некоторым устройствам IIb (MDR, статья 52 (4), 2-й параграф), для которых сводная информация о безопасности и клинических характеристиках еще не утверждена уполномоченным органом)</p> <p><input type="checkbox"/> Другое (укажите):</p> |
| SSCP-FS-2024<br>Редакция 1                                                          |                   | Обновлено за период с 1 января 2019 г. по 31 декабря 2024 г. | <p><input type="checkbox"/> Да</p> <p>Язык валидации: English</p> <p><input type="checkbox"/> Нет (применимо только к имплантируемым</p>                                                                                                                                                                                                                                                                             |

|                            |               |                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                    |
|----------------------------|---------------|-------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                            |               |                                                       | <p>устройствам класса Па или некоторым устройствам Пб (MDR, статья 52 (4), 2-й параграф), для которых сводная информация о безопасности и клинических характеристиках еще не утверждена уполномоченным органом)</p> <p><input type="checkbox"/> Другое (укажите):</p>                                                                                                                                              |
| SSCP-FS-2024<br>Редакция 2 | June 20, 2025 | Пересмотрено на основании запросов NSAI для валидации | <p><input checked="" type="checkbox"/> Да</p> <p>Язык валидации: English</p> <p><input type="checkbox"/> Нет (применимо только к имплантируемым устройствам класса Па или некоторым устройствам Пб (MDR, статья 52 (4), 2-й параграф), для которых сводная информация о безопасности и клинических характеристиках еще не утверждена уполномоченным органом)</p> <p><input type="checkbox"/> Другое (укажите):</p> |

**Súhrn údajov o bezpečnosti a klinickej účinnosti**  
**Cievny uzatvárací systém FemoSeal™ Vascular Closure System**

|                                                            |                                                                                              |
|------------------------------------------------------------|----------------------------------------------------------------------------------------------|
| <b>Výrobca</b>                                             | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 USA          |
| <b>SRN výrobcu</b>                                         | US-MF-000019594                                                                              |
| <b>Zástupca vedenia/PRRC</b>                               | Kimberly Feitl<br>Vice President, Quality                                                    |
| <b>Základný UDI-DI</b>                                     | 38970FS79                                                                                    |
| <b>Číslo EMDN</b>                                          | C900199 – Systémy hemostázy – iné                                                            |
| <b>Trieda pomôcky</b>                                      | Trieda III                                                                                   |
| <b>Rok, kedy bola pomôcka prvýkrát označená značkou CE</b> | 2005                                                                                         |
| <b>Zástupca pre EÚ</b>                                     | Terumo Europe N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgicko<br>SRN: BE-AR-000001433 |
| <b>Notifikovaný orgán</b>                                  | NSAI<br>CE 0050                                                                              |

## Obsah

|            |                                                                                            |          |
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Tento súhrn parametrov bezpečnosti a klinického výkonu (SSCP) je určený na to, aby poskytol verejný prístup k aktualizovanému súhrnu údajov o bezpečnosti a klinickej účinnosti cievneho uzatváracieho systému FemoSeal™ Vascular Closure System (VCS).

Súhrn parametrov bezpečnosti a klinického výkonu pomôcky určený pre používateľov/zdravotníckych pracovníkov je uvedený nižšie v **časti 1.0**.

## **1.0 SÚHRN PRE POUŽÍVATEĽOV/ZDRAVOTNÍCKYCH PRACOVNÍKOV**

SSCP nemá nahradiť návod na použitie, ktorý je hlavným dokumentom na zaistenie bezpečného používania pomôcky, ani nie je určený na poskytovanie diagnostických alebo terapeutických návrhov určeným používateľom alebo pacientom. SSCP tiež nenahrádza povinné informácie na kartách implantátov ani na akýchkoľvek iných povinných dokumentoch.

### **1.1 Určené použitie pomôcky**

#### **1.1.1 Určené použitie**

Cievny uzatvárací systém FemoSeal™ Vascular Closure System je zdravotnícka pomôcka určená na uzavretie arteriálnej punkcie po perkutánnej katetrizácii cez spoločnú femorálnu artériu.

#### **1.1.2 Indikácie na použitie**

Cievny uzatvárací systém FemoSeal™ Vascular Closure System je indikovaný na použitie pri uzatvorení bežnej femorálnej arteriálnej punkcie (arteriotómie) u pacientov, ktorí podstúpili perkutánnu katetrizáciu pomocou 7F (2,33 mm) alebo menšieho procedurálneho zavádzača.

#### **1.1.3 Kontraindikácie a/alebo obmedzenia**

Cievny uzatvárací systém FemoSeal™ Vascular Closure System je kontraindikovaný u pacientov s arteriotómiami, u ktorých sa používali zavádzače alebo pomôcky väčšie ako 7F (2,33 mm).

#### **1.1.4 Cieľová skupina používateľov**

Bezpečnosť a účinnosť cievneho uzatváracieho systému FemoSeal™ Vascular Closure System bola stanovená u pacientov vo veku 18 rokov a starších, ktorí podstúpili perkutánnu katetrizáciu pomocou 7F (2,33 mm) alebo menšieho procedurálneho zavádzača.

#### **1.1.5 Osobitné skupiny pacientov**

Bezpečnosť a účinnosť cievneho uzatváracieho systému FemoSeal™ Vascular Closure System nebola stanovená u nasledujúcich skupín pacientov:

- pacienti s existujúcim autoimunitným ochorením,
- pacienti podstupujúci terapeutickú trombolýzu,
- pacienti s klinicky významným ochorením periférnych ciev,
- pacienti s nekontrolovanou hypertenziou (> 220 mmHg systolický alebo > 110 mmHg diastolický tlak),
- pacienti s poruchou krvácania vrátane trombocytopenie (< 100 000 počet trombocytov) alebo anémie (Hgb < 10 mg/dl),

- pacienti s vnútorným lúmenom spoločnej femorálnej artérie menším ako 5 mm,
- pacienti s poruchou funkcie obličiek a/alebo pečene,
- pacienti s inou relevantnou komorbiditou,
- populácia so špecifickým rasovým a/alebo etnickým pôvodom,
- pacienti s infarktom myokardu v priebehu 72 hodín,
- pacienti s cievnyňm štepom alebo stentom v mieste vpichu,
- tehotné alebo dojčiacie ženy,
- pacienti vo veku do 18 rokov.

### 1.1.6 Určení používateľa

Určeními používateľmi cievneho uzatváracieho systému FemoSeal™ Vascular Closure System sú lekári vyškolení na vykonávanie arteriálneho prístupu a uzatváranie endovaskulárnych zákrokov prostredníctvom spoločnej femorálnej artérie a zúčastnili sa školenia lekárov o používaní pomôcky FemoSeal™ od spoločnosti Terumo Medical Corporation.

## 1.2 Opis pomôcky

### 1.2.1 Opis pomôcky

Cievny uzatvárací systém FemoSeal™ Vascular Closure System, ktorý vyrába spoločnosť Terumo Medical Corporation (TMC), je vstrebateľná pomôcka na uzatváranie ciev určená na dosiahnutie arteriálnej hemostázy po perkutánnej katetrizácii pomocou spoločnej femorálnej artérie.

Uzatváracie prvky FemoSeal™ pozostávajú z dvoch vstrebateľných polymérových diskov, vnútorného uzáveru a vonkajšieho uzamykacieho disku, ktoré sú navzájom spojené vstrebateľným polyfilom, čím mechanicky uzatvárajú arteriotómiu (pozri **obrázok 1.1** a **obrázok 1.2**). Po zavedení cez zavádzač s kužeľovým puzdrom je vonkajší uzamykací disk nasadený na teleso polyfilu, čo vedie k mechanickému uzavretiu miesta vpichu medzi vnútorným a vonkajším uzamykacím diskom. Vnútorný uzáver a vonkajší uzamykací disk sú fixované trením na telese polyfilu. Hemostáza sa dosahuje mechanickými prostriedkami. Uzatváracie prvky sa rozkladajú hydrolýzou.

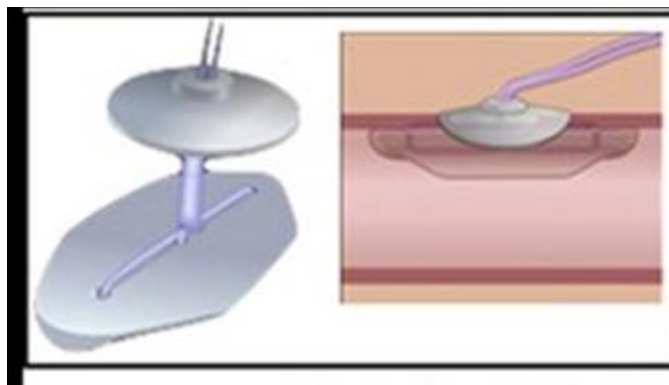
Implantovateľné uzatváracie komponenty, vnútorný uzáver a vonkajší uzamykací disk sa rozložia za osemnásť (18) mesiacov, pričom polyfil sa rozloží a absorbuje prostredníctvom hydrolýzy okolitým tkanivom po približne dvoch (2) až troch (3) rokoch. Schopnosť implantovateľných uzatváracích komponentov udržiavať kompresiu na arteriotómii bola testovaná až osem (8) hodín.

Produkty rozkladu sa metabolizujú a vylučujú v moči alebo sa vylúčia ako oxid uhličitý cez pľúca. v štúdiách na zvieratách neboli pozorované žiadne akumulčné účinky. Ďalšie komponenty pomôcky FemoSeal™, ktoré sa počas zákroku dostanú do kontaktu s tkanivom alebo krvou, sú zavádzač s kužeľovým puzdrom, dilatátor, zatláčacia hadička, zatláčací piest a vodiaci drôt.

**Obrázok 1.1 Vnútrotný uzáver a vonkajší uzamykací disk**



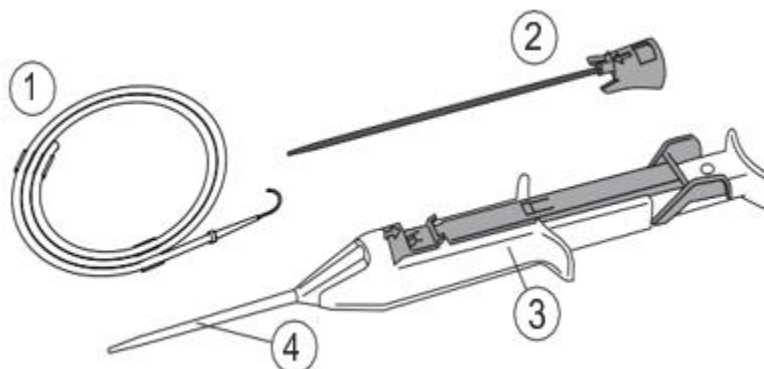
**Obrázok 1.2 Zavedený vnútrotný uzáver a vonkajší uzamykací disk**



Jednotka FemoSeal™ je balená spolu s dilatátorom a vodiacim drôtom s vonkajším priemerom 0,038" (0,97 mm) a dĺžkou 27,5" (70 cm) a vyrovnávačom „J“, pozri **obrázok 1.3** nižšie.

Vodiaci drôt sa nachádza vo vnútri polyetylénovej hadičky. Všetky časti sú zabalené na pevnom papierovom podklade. Balenie obsahuje aj kartu implantátu pacienta. Cievny uzatvárací systém FemoSeal™ Vascular Closure System na riadne fungovanie nevyžaduje ďalšie príslušenstvo, pričom táto pomôcka je určená len na použitie s dilatátorom a vodiacim drôtom, ktorý je súčasťou balenia produktu.

**Obrázok 1.3 Jednotka FemoSeal™ VCS s vodiacim drôtom a dilatátorom**



### 1.2.2 Suroviny a komponenty

V tabuľke 1.1 nižšie sú uvedené komponenty pomôcky FemoSeal™ VCS.

**Tabuľka 1.1 Materiály a komponenty pomôcky FemoSeal™ VCS**

| Číslo dielu | Opis                                                                               |                                                            | Materiál                                                                                                                                                                                               |
|-------------|------------------------------------------------------------------------------------|------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1           | Vodiaci drôt 0,038" (0,97 mm) s vodiacim drôtom a vyrovnávačom „J“ vodiaceho drôtu |                                                            | Vodiaci drôt: Nerezová oceľ 304<br><br>Vyrovnávač „J“: Polypropylén, fialový pigment<br><br>Spona: Polyetylén<br><br>Hadička: Polyetylén                                                               |
| 2           | Dilatátor FemoSeal™                                                                |                                                            | Hrdlo: Tetrahydrofurán, modrý pigment, polybutyléntereftalát (PBT)<br><br>Hadička: Polyetylén s vysokou hustotou (HDPE), čierny pigment<br><br>Lubrikant: Silikón Dow Corning 360                      |
| 3/4         | Jednotka FemoSeal                                                                  | Tvarované RD7 – vnútorný uzáver a vonkajší uzamykací disk* | Kopolymér medzi glykolidom, trimetylkarbonátom, ε-kaprolaktónom a TMP: trimetylpropánom (iniciátor)                                                                                                    |
|             |                                                                                    | Polyfil *                                                  | Segmentovaný kopolymér medzi L, L-laktidom, trimetyléncarbonátom, ε-kaprolaktónom a 1,3 propanediólom (iniciátorom)<br><br>Povrchová úprava je kopolymér medzi glykolidom, ε-kaprolaktónom a L-lyzínom |

|  |  |                              |                                                |
|--|--|------------------------------|------------------------------------------------|
|  |  | Zatlačacia hadička           | Polypropylén                                   |
|  |  | Zatlačací piest              | Nerezová oceľ 304V                             |
|  |  | Posúvač                      | Polybutyléntereftalát (PBT)                    |
|  |  | Kryt                         | Polybutyléntereftalát (PBT)                    |
|  |  | Tlačidlo                     | Polybutyléntereftalát (PBT)                    |
|  |  | Veko tlačidla                | Polyoxymetylén (POM)/polyacetálový kopolymér   |
|  |  | Puzdro                       | Polybutyléntereftalát (PBT)                    |
|  |  | Dištančný prvok              | Polybutyléntereftalát (PBT)                    |
|  |  | Kužel                        | Polypropylén                                   |
|  |  | Veko krytu                   | Polybutyléntereftalát (PBT)                    |
|  |  | Bezpečnostná poistka         | Polybutyléntereftalát (PBT), modrý pigment     |
|  |  | Veko puzdra                  | Polybutyléntereftalát (PBT)                    |
|  |  | Tesnenie hadičky             | Silikónová rozperka a 70                       |
|  |  | Tesnenie krytu               | Silikónová rozperka a 50                       |
|  |  | Pružina                      | Nerezová oceľ 302                              |
|  |  | Zavádzač s kužeľovým puzdrom | Polypropylén<br>Silikón Dow Corning 360, hexán |

\* Implantovateľná časť pomôcky; implantovateľné komponenty sú bezpečné pri použití v prostredí MRI

FemoSeal™ VCS sa sterilizuje pomocou etylénoxidu (EO) a je to jednorazová zdravotnícka pomôcka. Pomôcka FemoSeal™ VCS je navrhnutá tak, aby sa nedala opätovne použiť.

### **Spôsob fungovania**

FemoSeal™ VCS podporuje mechanickú hemostázu nasadením implantovateľných uzatváracích prvkov vo vnútri a mimo spoločnej femorálnej artérie. Mechanizmus zabraňujúci krvácaniu je zabezpečený vnútorným uzáverom, ktoré utesňuje miesto vpichu, a vonkajším uzamykacím diskom, ktorý udržiava vnútorné tesnenie na mieste.

### **1.2.3 Klinický prínos**

FemoSeal™ VCS poskytuje nasledujúce klinické prínosy vo vzťahu k vaskulárnemu uzáveru po punkcii spoločnej femorálnej artérie:

- Skrátene čas do hemostázy<sup>1</sup>
- Skrátene čas do ambulácie<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

#### 1.2.4 Predchádzajúca(-e) generácia(-e) alebo varianty

- Prvá verzia pomôcky FemoSeal™ VCS (č. 11200) sa na európskom trhu predávala v roku 2005 a sčasti v roku 2006.
- Súčasný systém FemoSeal™ VCS (č. 11202) s vylepšeným zavádzacím systémom je na trhu od 28. marca 2006.

#### 1.2.5 Príslušenstvo určené na použitie v kombinácii s pomôckou

Jednotka FemoSeal™ je balená spolu s dilatátorom a 0,038" (0,97 mm) OD, vodiacim drôtom s dĺžkou 27,5" (70 cm) a vyrovnávačom „J“. Vodiaci drôt je príslušenstvom k jednotke FemoSeal™. Vyrovnávač „J“ je súčasťou vodiaceho drôtu, zatiaľ čo dilatátor je súčasťou jednotky FemoSeal™. Vodiaci drôt je jediným uvažovaným príslušenstvom. Vodiaci drôt sa nachádza vo vnútri polyetylénovej hadičky. Všetky časti sú zabalené na pevnom papierovom podklade. Balenie obsahuje aj kartu implantátu pacienta. Cievny uzatvárací systém FemoSeal™ Vascular Closure System na riadne fungovanie nevyžaduje ďalšie príslušenstvo, pričom táto pomôcka je určená len na použitie s dilatátorom a vodiacim drôtom, ktorý je súčasťou balenia produktu.

#### 1.2.6 Ďalšie pomôcky a výrobky určené na použitie v kombinácii s pomôckou

Pomôcka FemoSeal™ VCS nevyžaduje na riadne fungovanie ďalšie pomôcky.

### 1.3 Riziká a varovania

#### 1.3.1 Reziduálne riziká a nežiaduce účinky

Známe alebo predvídateľné nežiaduce udalosti, poškodenia a komplikácie spojené s používaním pomôcky FemoSeal™ VCS v dôsledku zvýšeného rizika sú uvedené v **tabuľke 1.2**. Miera výskytu je založená na analýze dokumentácie rizík a vypočítaná na základe údajov z dohľadu po uvedení na trh od 1. septembra 2019 do 31. augusta 2024. Pre pomôcku FemoSeal™ VCS neexistujú žiadne neznáme reziduálne riziká a všetky aplikovateľné riziká sa riešia v návode na použitie a procese riadenia rizík.

**Tabuľka 1.2. Nežiaduce udalosti/komplikácie spojené s pomôckou FemoSeal**

| Škodlivé následky                       | Miera výskytu (%) | Zmierňujúce faktory                                                                                                                                                                  |
|-----------------------------------------|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Alergická reakcia                       | 0,0000            | Činnosti a plány na zníženie rizika na čo najnižšiu úroveň rizika boli riešené prostredníctvom konštrukčných prvkov výrobku, výrobných smerníc, označenia výrobku a školení lekárov. |
| Aneuryzma                               | 0,0000            |                                                                                                                                                                                      |
| AV fistula                              | 0,0001            |                                                                                                                                                                                      |
| Strata krvi/krvácanie                   | 0,0280            |                                                                                                                                                                                      |
| Smrť                                    | 0,0002            |                                                                                                                                                                                      |
| Ekchymóza                               | 0,0000            |                                                                                                                                                                                      |
| Embólia                                 | 0,0000            |                                                                                                                                                                                      |
| Reakcia na cudzie teleso                | 0,0000            |                                                                                                                                                                                      |
| Hematóm                                 | 0,0027            |                                                                                                                                                                                      |
| Hemorágia                               | 0,0001            |                                                                                                                                                                                      |
| Infekcia                                | 0,0002            |                                                                                                                                                                                      |
| Zápalová reakcia                        | 0,0000            |                                                                                                                                                                                      |
| Pocit necitlivosti                      | 0,0000            |                                                                                                                                                                                      |
| Bolesť                                  | 0,0000            |                                                                                                                                                                                      |
| Nepříjemné pocity u pacienta            | 0,0004            |                                                                                                                                                                                      |
| Odloženie zákroku                       | 0,0065            |                                                                                                                                                                                      |
| Pseudoaneuryzma                         | 0,0004            |                                                                                                                                                                                      |
| Retroperitoneálne krvácanie             | 0,0002            |                                                                                                                                                                                      |
| Sepsa                                   | 0,0000            |                                                                                                                                                                                      |
| Trombembólia                            | 0,0000            |                                                                                                                                                                                      |
| Trombóza                                | 0,0001            |                                                                                                                                                                                      |
| Oklúzia cievy/ischémia dolnej končatiny | 0,0002            |                                                                                                                                                                                      |
| Perforácia cievy                        | 0,0000            |                                                                                                                                                                                      |
| Disekcia/lacerácia cievneho tkaniva     | 0,0003            |                                                                                                                                                                                      |



### 1.3.2 Varovania a bezpečnostné opatrenia

#### Varovania

1. Nepoužívajte, ak je balenie poškodené, alebo v prípade, že sterilná bariéra je porušená.
2. Nepoužívajte po dátume expirácie – biologicky degradovateľné časti by mohli fungovať nesprávne.
3. Nepoužívajte, ak sa akákoľvek časť zdá byť poškodená alebo chybná.
4. Použitie cievneho uzatváracieho systému FemoSeal™ Vascular Closure System tam, kde by mohlo dôjsť k bakteriálnej kontaminácii procedurálneho zavádzача alebo okolitých tkanív, by mohlo spôsobiť vznik infekcie.
5. Ak je podozrenie, že bola prepichnutá zadná stena tepny, alebo bol vytvorený viac ako jeden vpich tepny, nespoliehajte sa výhradne na cievny uzatvárací systém FemoSeal™ Vascular Closure System, aby ste dosiahli arteriálnu hemostázu. Použite ďalšiu manuálnu alebo mechanickú kompresiu.
6. Ak je miesto vpichu na úrovni bifurkácie femorálnej artérie alebo distálne k nej, cievny uzatvárací systém FemoSeal™ Vascular Closure System by sa nemal používať v dôsledku rizika nesprávneho umiestnenia vnútorného uzáveru. Táto udalosť by mohla spôsobiť krvácané komplikácie a/alebo narušenie normálneho prietoku krvi.
7. Ak z miesta incízie pretrváva arteriálne krvácanie, neskracujte polyfil, až kým nebude dosiahnutá hemostáza. Ak nie je hemostáza dosiahnutá, utiahnite polyfil sterilným krytím na rany a aplikujte doplnkovú kompresiu až do dosiahnutia hemostázy. v prípade pretrvávajúceho arteriálneho krvácania sa môžu objaviť významné krvácané komplikácie, ktoré by mohli spôsobiť poranenie pacienta alebo jeho smrť.
8. Nepoužívajte cievny uzatvárací systém FemoSeal™ Vascular Closure System, ak je miesto vpichu proximálne k inguinálnemu väzu, pretože to môže spôsobiť retroperitoneálny hematóm.
9. Pacienti s vyšším rizikom krvácania môže dôjsť k zvýšenej strate krvi, ktorá si vyžaduje transfúziu.
10. Ak sa vnútorný disk oddelí, môže potenciálne spôsobiť trombotickú a/alebo embolickú príhodu.

#### Bezpečnostné opatrenia

1. Postup zavedenia cievneho uzatváracieho systému FemoSeal™ Vascular Closure System by mal byť uskutočnený iba lekármi adekvátne vyškolenými na použitie tejto pomôcky.
2. Pred zavedením cievneho uzatváracieho systému FemoSeal™ Vascular Closure System urobte čiastočný femorálny angiogram alebo ultrazvukovo riadenú femorálnu punkciu.

3. Prerušte zákrok ak:
  - Priemer lúmenu spoločnej femorálnej artérie < 5 mm.
  - Ste zaznamenali prítomnosť stenózy alebo významného plátu v blízkosti miesta vpichu spoločnej femorálnej artérie.
  - Arteriálna punkcia je na úrovni bifurkácie femorálnej artérie alebo distálne k nej.
  - V blízkosti miesta vpichu spoločnej femorálnej artérie sa nachádzajú anomálne vetvy alebo abnormality ciev.
4. Ak je prítomný akýkoľvek hematóm, je potrebné venovať zvláštnu opatrnosť pri zavádzaní zavádzača s kužeľovým puzdrom do artérie.
5. Používajte techniku punkcie jednej steny. Neprepichujte zadnú stenu artérie.
6. Pri používaní cievneho uzatváracieho systému FemoSeal™ Vascular Closure System vždy dodržiavajte sterilnú techniku.
7. Cievny uzatvárací systém FemoSeal™ Vascular Closure System je určený len na jedno použitie a nesmie sa resterilizovať alebo opakovane akýmkoľvek spôsobom používať. Jednotka FemoSeal™ je navrhnutá tak, aby sa nedala znova použiť.
8. Ak pri zavádzaní vnútorného uzáveru pocítite neočakávaný odpor, zákrok prerušte.
9. Pre správne nasadenie vnútorného uzáveru posuňte palec tak, aby tlačidlo mohlo voľne vyskočiť späť.
10. Pred zavedením vonkajšieho uzamykacieho disku skontrolujte, či je hrot zavádzača s kužeľovým puzdrom pomôcky FemoSeal™ pod povrchom kože. Vonkajší uzamykací disk môže byť nechtiac umiestnený nad povrch kože najmä u pacientov s malou vzdialenosťou medzi femorálnou artériou a povrchom kože.
11. Na správne zavedenie môže byť potrebná kožná incízia.
12. Ak je vnútorný uzáver v tepne, ale nie je možné celkom stlačiť tlačidlo a umiestniť vonkajší uzamykací disk, môže si odstránenie uzatváracích prvkov FemoSeal™ Vascular Closure System vyžadovať operáciu.
13. Ak bude potrebný opätovný vpich do tej istej femorálnej artérie v priebehu 18 mesiacov, mal by sa vykonať aspoň jeden centimeter proximálne k predchádzajúcemu prístupovému miestu pomôcky FemoSeal™ Vascular Closure System.
14. Poučte pacienta, aby postupoval podľa pokynov lekára týkajúcich sa kontroly miesta uzavretia.
15. Poučte pacienta, aby po dobu nasledujúcich 18 mesiacov nosil informačnú kartu pacienta.

### **Bezpečnostné opatrenia pri prepúšťaní**

Pred prepustením vyšetrite pacienta z hľadiska prítomnosti nasledujúcich klinických stavov:

1. Krvácanie a/alebo hematóm v mieste uzavretia.
2. Bolesť pri chôdzi.
3. Príznaky infekcie v mieste uzavretia.

### **1.3.3 Bezpečnostné nápravné opatrenia**

Počas obdobia od 1. septembra 2019 do 31. augusta 2024 došlo k jednému bezpečnostnému nápravnému opatreniu zahŕňajúcemu pomôcku FemoSeal™ VCS.

V roku 2022 spoločnosť Terumo dobrovoľne stiahla pomôcku FemoSeal™ VCS z dôvodu sťažností týkajúcich sa zlyhaní testovania procesu a uvoľnenia šarže výrobku FemoSeal vyrobenej spoločnosťou Elkton týkajúceho sa merania zatlačacej a retrakčnej sily. z Južnej Kórey bolo stiahnutých celkovo 950 kusov.

## **1.4 Klinické hodnotenie a klinické sledovanie po uvedení na trh**

**Tabuľka 1.3** obsahuje zoznam pivotných štúdií zahrnutých do uvedenia VCS FemoSeal™ na trh, ako aj štúdie po uvedení na trh a činnosti klinického sledovania po uvedení na trh. Verzia pomôcky použitá v štúdiu je uvedená v nasledujúcej tabuľke. Prvá verzia FemoSeal™ VCS (č. 11200) bola na trhu do roku 2006, ďalšia verzia (č. C11202), ktorá je v súčasnosti na trhu, bola uvedená v roku 2006.

**Tabuľka 1.3 Zhrnutie pivotných štúdií**

| <b>Test funkčnosti na zvieratách pred uvedením na trh</b>                                                                                                                                                                                                               | <b>Verzia pomôcky</b> |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                 |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                 |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                 |
| <b>Prvá klinická štúdia na ľuďoch</b>                                                                                                                                                                                                                                   |                       |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                 |

| Dokončené klinické štúdie po uvedení na trh                                                                                     |                              |
|---------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                      | C11202<br>(aktuálna pomôcka) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                               | C11202<br>(aktuálna pomôcka) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | C11202<br>(aktuálna pomôcka) |
| The FemoSeal Vascular Closure System (VCS) Registry: a Prospective, Multi-Center, Observational Study in Europe (2022)          | C11202<br>(aktuálna pomôcka) |
| Plánované/prebiehajúce klinické štúdie po uvedení na trh                                                                        |                              |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                      | C11202<br>(aktuálna pomôcka) |
| Činnosti klinického sledovania po uvedení na trh                                                                                |                              |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(aktuálna pomôcka) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(aktuálna pomôcka) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(aktuálna pomôcka) |

#### 1.4.1 Zhrnutie údajov z testovania na zvieratách a klinických skúšaní pred uvedením na trh

V tabuľke 1.4 nižšie sú opísané všetky štúdie pred uvedením na trh, testovania na zvieratách aj klinické skúšania.

**Tabuľka 1.4 Zhrnutia štúdií pred uvedením na trh**

| Test funkčnosti na zvieratách pred uvedením na trh                                                                 |                                   |                                              |                                                                                                                          |                                                                                                           |                                                                                                                                                                               |
|--------------------------------------------------------------------------------------------------------------------|-----------------------------------|----------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Názov štúdie                                                                                                       | Rok / CI                          | Typ štúdie                                   | Ciele                                                                                                                    | Medzníky                                                                                                  | Potenciálne kritériá akceptácie                                                                                                                                               |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. | 2000<br>Radi Medical<br>System AB | Štúdia na zvieratách;<br>Prieskumné skúmanie | Cieľom štúdie bolo zhodnotenie biokompatibility a biologickej funkčnosti biologicky odbúrateľného implantátu určeného na | N = 3 dospelé samice ovce, 1 zviera na časový bod<br><br>Následná histopatologická analýza, makroskopické | Arteriálna priechodnosť<br>• Vyhodnotenie prietoku krvi po zavedení – 2/3 zníženie prietoku krvi spojené s dočasným arteriálnym vazospazmom, ktorý bol pripísaný zákroku, oba |

|                                                                                                                                                      |                                             |  |                                                                                                                          |                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------|--|--------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | Vykonané spoločnosťou Biomatech, Francúzsko |  | dosiahnutie hemostázy v cievnom systéme. Správa sa zaoberá rezervnými zvieratami zo štúdie č. 862 (č. dokumentu 1051-01) | <p>hodnotenie a ultraštruktúrálna analýza</p> <ul style="list-style-type: none"> <li>12 mesiacov</li> <li>15 mesiacov</li> <li>18 mesiacov</li> </ul> <p>Sledovanie farebným dopplerovským ultrazvukom – následná kontrola po 30 dňoch v miestach karotického a femorálneho arteriálneho prístupu</p> | <p>sa vyskytli na ľavej spoločnej karotickej artérii</p> <ul style="list-style-type: none"> <li>Sledovanie farebným dopplerovským ultrazvukom (4 týždne) – 3/3 (100 %) bez významnejšieho zníženia prietoku krvi 30 dní po implantácii</li> <li>Makroskopické pozorovania <ul style="list-style-type: none"> <li>12 mesiacov – makroskopicky potvrdená priechodnosť bez anatomickej viditeľných oklúzií; žiadne makroskopické lézie lokálnej intolerancie (hemorágia, nekroza alebo neovaskularizácia); enkapsulácia vnútorného disku sa javí ako výrazná</li> <li>15 mesiacov – makroskopické pozorovanie nepreukázalo žiadne príznaky zápalu; nezistili sa žiadne zvyšky vnútorných alebo vonkajších diskov; enkapsulácia tkaniva nachádzajúceho sa v oblasti vonkajšieho disku sa javila rovnaká ako po 12 mesiacoch pozorovania</li> <li>18 mesiacov – makroskopické pozorovanie nepreukázalo žiadne príznaky lokálnej intolerancie, vonkajší disk je viditeľný (3/3 prípady), rozloženie vnútorného disku kompletne; 1/3 (ľavá spoločná karotická artéria) – depresia steny tepny pozorovaná v mieste implantácie (môže súvisieť s použitím pomôcky)</li> </ul> </li> <li>Záver <ul style="list-style-type: none"> <li>Makroskopicky sa 12, 15 a 18 mesiacov po implantácii nezistili žiadne nekrotické, degeneratívne ani trombotické príznaky.</li> </ul> </li> </ul> |
|------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------|--|--------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

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|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|-------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                                                                                         |                                                                                |                                           |                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                         | <ul style="list-style-type: none"> <li>Zdá sa, že proces odbúravania vnútorných a vonkajších diskov postupoval medzi 12. a 18. mesiacom a v 18. mesiaci bol dokončený, pričom implantovanú oblasť pokrývalo belavé tkanivo.</li> <li>Histologicky po 18 mesiacoch už nebol viditeľný polymérny materiál, bolo však prítomné endoluminálne fibrózne tkanivo. Neboli zaznamenané žiadne nekrotické, degeneratívne ani trombotické lézie.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 2002 Radi Medical System AB<br><br>Vykonané spoločnosťou Biomatech, Francúzsko | Štúdia na zvieratách; Prieskumné skúmanie | Cieľom štúdie bolo zhodnotenie biokompatibility biologicky odbúrateľného implantátu určeného na dosiahnutie hemostázy v cievnom systéme. | <p>Následné kontroly (po implantácii)</p> <ul style="list-style-type: none"> <li>12 týždňov</li> <li>24 týždňov</li> <li>36 týždňov</li> </ul> <p>N = 12 oviec, 3 zvieratá na časový bod, 3 rezervné zvieratá utratené po 12, 15 a 18 mesiacoch</p> <p>Implantačné miesta – pravá a ľavá femorálna artéria, pravá a ľavá spoločná karotická artéria</p> <p>Analýza farebným dopplerovým ultrazvukom</p> | <p><u>Priechodnosť karotických a femorálnych artérií po 4 týždňoch</u></p> <ul style="list-style-type: none"> <li>Významné zníženie prietoku krvi 0/12 (0 %)</li> </ul> <p><u>Žiadne významné zníženie prietoku krvi</u></p> <ul style="list-style-type: none"> <li>Závažné obmedzenie prietoku krvi v súvislosti so zavedením pomôcky 0/12 (0 %)</li> <li>Zníženie prietoku krvi v ľavej spoločnej karotíde 2/12 (16,6 %) v dôsledku dočasného arteriálneho vazospazmu (súvisí s chirurgickým zákrokom, nie s pomôckou)</li> </ul> <p><u>Zhoršenie prietoku krvi zistené počas následnej kontroly</u></p> <p>12 týždňov – 0/12 (0 %)<br/>24 týždňov – 0/12 (0 %)<br/>36 týždňov – 0/12 (0 %)</p> <p>Meranie krvného tlaku (3 ovce – 36 týždňov)</p> <ul style="list-style-type: none"> <li>Nebol zistený žiadny významný pokles krvného prietoku</li> </ul> <p>Makroskopické údaje na integráciu a rozloženie (stupeň 0 – 4)</p> |

|  |  |  |  |  | <p><u>Karotické oblasti</u></p> <p><u>Vnútorná časť</u></p> <p>– enkapsulácia</p> <p>12. týždeň 1,3</p> <p>24. týždeň 0,8</p> <p>36. týždeň 0,7</p> <p>– odbúravanie materiálu</p> <p>12. týždeň 2,2</p> <p>24. týždeň 2,3</p> <p>36. týždeň 0,7</p> <p><u>Vonkajšia strana</u></p> <p>– enkapsulácia</p> <p>12. týždeň 2,0</p> <p>24. týždeň 1,0</p> <p>36 týždňov 0,8</p> <p>– odbúravanie materiálu</p> <p>12. týždeň 2,0</p> <p>24. týždeň 2,7</p> <p>36. týždeň 3,2</p> <p><u>Femorálne oblasti</u></p> <p><u>Vonkajšia strana</u></p> <p>– enkapsulácia</p> <p>12. týždeň 1,0</p> <p>24. týždeň 2,7</p> <p>36. týždeň 1,0</p> <p>– odbúravanie materiálu</p> <p>12. týždeň 2,0</p> <p>24. týždeň 2,4</p> <p>36. týždeň 3,0</p> <p><u>Vnútorná časť</u></p> <p>– enkapsulácia</p> <p>12. týždeň 2,0</p> <p>24. týždeň 1,2</p> <p>36. týždeň 1,0</p> <p>– odbúravanie materiálu</p> <p>12. týždeň 1,0</p> <p>24. týždeň 2,2</p> <p>36. týždeň 3,0</p> <p><u>Histologické údaje pre integráciu, odbúravanie a zápalové markery (medián príslušných hodnôt, index 0 – 4) n = 6</u></p> <p><u>Karotické oblasti</u></p> <p>Externá fibróza</p> <p>12 týždňov – 2,3</p> <p>24 týždňov – 2,3</p> |
|--|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | 36 týždňov – 1,8<br>Vnútorná neointima<br>12 týždňov – 3,0<br>24 týždňov – 2,7<br>36 týždňov – 3,3<br>Odbúravanie materiálu<br>12 týždňov – 1,7<br>24 týždňov – 3,0<br>36 týždňov – 3 +<br>Zápalové markery<br>(makrofágy)<br>12 týždňov – 3,0<br>24 týždňov – 1,7<br>36 týždňov – 1,7<br><u>Femorálne oblasti</u><br>Externá fibróza<br>12 týždňov – 1,3<br>24 týždňov – 1,5<br>36 týždňov – 1,7<br>Vnútorná neointima<br>12 týždňov – 3,7<br>24 týždňov – 3,3<br>36 týždňov – 3,8<br>Odbúravanie materiálu<br>12 týždňov – 2,0<br>24 týždňov – 3,0<br>36 týždňov – 3 +<br>Zápalové markery<br>(makrofágy)<br>12 týždňov – 3,5<br>24 týždňov – 1,8<br>36 týždňov – 1,8<br><br><u>Hodnoty histomorfologickej</u><br><u>priechodnosti</u><br>Karotické oblasti<br>12 týždňov – 74,0 %<br>24 týždňov – 81,9 %<br>36 týždňov – 89,43 %<br>Femorálne oblasti<br>12 týždňov – 42,2 %<br>24 týždňov – 73,21 %<br>36 týždňov – 78,71 %<br><br><u>Priechodnosť ciev na</u><br><u>ultrazvuku (v %)</u><br>Karotická oblasť<br>12. týždeň – 94,6 %<br>24. týždeň – 96,7 %<br>36. týždeň – 94,7 %<br>Femorálne oblasti |
|--|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|



|                                                                                                                                                                                                                                                                 |                                                                                       |                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                                                                                 |                                                                                       |                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                        | 12. týždeň – 66,9 %<br>24. týždeň – 63,6 %<br>36. týždeň – 75,1 %<br><br>Záver <ul style="list-style-type: none"> <li>Nebola zistená žiadna výrazná lokálna intolerancia (absencia viditeľných zápalových, nekrotických alebo degeneratívnych lézií) po 12, 24 alebo 36 týždňoch</li> <li>Nebola zaznamenaná žiadna významná nežiaduca reakcia tkanív vzhľadom na hostiteľa a pomôcku</li> <li>Odbúravanie implantátu bolo po 36 týždňoch takmer dokončené</li> </ul>                                                                                                                                                                                                |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France). | 2002<br><br>Radi Medical System AB<br><br>Vykonané spoločnosťou Biomatech, Francúzsko | Štúdia na zvieratách | Cieľ štúdie bolo zhodnotenie biokompatibility a biofunkčnosti biologicky odbúrateľného implantátu určeného na dosiahnutie hemostázy v cievnom systéme. Skúšaná pomôcka bola určená na vstup do otvoru punkcie v artériách na dosiahnutie hemostázy. Jeden disk bol zavedený do otvoru punkcie v artérii a druhý utiahol vnútorný disk z vonkajšej strany artérie. Oba disky boli zavedené cez plášť závaždača. Tieto disky boli navrhnuté tak, aby zabráňovali krvácaniu, zahojili sa do steny cievy a nakoniec sa rozpadli a absorbovali. Štúdia bola navrhnutá tak, aby zhromažďovala a analyzovala údaje po funkčnej implantácii do oviec a ošípaných na vyhodnotenie kapacity implantátu zachovať fyziologické funkcie pri použití v obehovom | Obdobie implantácie/následné kontroly sú po 5 týždňoch pre všetky zvieratá<br><br>4 ovce, 1 ošípaná<br><br>14 uzatváracích prvkov<br><br>8 uzatváracích prvkov implantovaných 2 ovciam<br><br>2 uzatváracie prvky implantované 1 ošípanej<br><br>Ak boli dva uzatváracie prvky implantované do tej istej femorálnej artérie, boli implantované vo vzdialenosti > 30 mm | Zaznamenali sa všetky kritériá nežiaducich príznakov (zápal, nekróza, krvácanie alebo ťubovoľné iné lézie) alebo akékoľvek vytvorenie tenkej pseudointimálnej vrstvy. Osobitná pozornosť bola venovaná počiatočnej integrácii pomôcky s tkanivom so špeciálnym dôrazom na vnútornú enkapsuláciu disku.<br><br>Makroskopicky sa nepozorovali žiadne významné príznaky lokálnej intolerance ani tvorby trombov. Makroskopické pozorovanie neodhalilo po implantácii uzatváracích prvkov vo femorálnych artériách žiadny rozdiel medzi ovcami a ošípanou. Makroskopicky sa nepozorovali žiadne významné príznaky lokálnej intolerance ani tvorby trombov. Makroskopické |

|  |  |  | <p>systéme, na určenie reakcie hostiteľa a reakcie pomôcky (fyzická neporušenosť, enkapsulácia do tkaniva v čase utratenia) a na vyhodnotenie rozloženia implantátu</p> |  | <p>pozorovanie neodhalilo po implantácii uzatváracích prvkov vo femorálnych artériách žiadny rozdiel medzi ovcami a ošípanou.</p> <p>Histopatologická analýza miesta implantácie u oviec nepreukázala žiadne lokálne nežiaduce reakcie. Vnútorne a vonkajšie disky vykazovali známky rozkladu a v niektorých prípadoch sa rozpadli na menšie časti. Vnútorne disky boli úplne integrované do neointimálneho tkaniva. Histopatologická analýza u ošípanej preukázala okolo vnútorných a vonkajších diskov o niečo viac zápalových znakov. U oboch zvierat vykazoval polyfil mierne viac zápalových znakov ako materiál disku, čo je pri pletenom šití normálne z dôvodu väčšej plochy povrchu.</p> <p>Priechodnosť cievy sa merala po 5 týždňoch použitím troch rôznych metód, histomorfometrickej, histomorfometrickej v kombinácii s meraním priemeru cievy pomocou posuvného meradla a pomocou farebnej dopplerovej ultrasonografie. Priemerná priechodnosť cievy u oviec bola od 60 do 80 % v závislosti od metódy (12 pozorovaní). U ošípanej bola priemerná priechodnosť cievy</p> |
|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                                                                                                                                                                                                              |                              |                                                 |                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                       | v rozmedzí od 40 do 80 %<br>(2 pozorovania).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Prvá klinická štúdia na ľuďoch</b>                                                                                                                                                                        |                              |                                                 |                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Názov štúdie                                                                                                                                                                                                 | Rok / CI                     | Typ štúdie                                      | Ciele                                                                                                                                                                                                                                                                                                                   | Medzníky                                                                                                                                                                                                                                                                                                                                                                              | Potenciálne kritériá akceptácie                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Otvorená, jednoskupinovú, multicentrickú štúdia | Cieľ štúdie bolo zistiť bezpečnosť, výkonnosť a účinnosť cievneho uzatváracieho systému FemoSeal Vascular Closure System (systém FemoSeal) vo všeobecnosti a konkrétne pre uzatváracie prvky u pacientov podstupujúcich diagnostické alebo intervenčné kardiologické zákroky s použitím prístupu cez femorálnu artériu. | Štúdia pozostávajúca z 2 častí<br><br>Celkom n = 80<br>1. časť n = 20<br>2. časť n = 60<br><br>Indikácie:<br>1. časť – diagnostická katetrizácia srdca s použitím femorálnej artérie ako prístupového bodu<br><br>2. časť – pacienti podstupujúci diagnostické a intervenčné srdcové zákroky s použitím femorálnej artérie ako prístupového bodu<br><br>Následná kontrola po 30 dňoch | Výsledky<br>– <u>hemostáza dosiahnutá s FS bez kompresie</u><br>– 1. časť 20/20 (100 %)<br>– 2. časť 58/60 (97 %)<br><br>Medián času do hemostázy v čase zákroku (2. časť) – 1,0 minúty (rozsah ihneď – 8 minút)<br><br><u>Čas do ambulácie (minúty)</u><br>1. časť –<br>Medián: 33,0<br>medián: 67,8<br>2. časť –<br>medián: 45<br>medián: 87,5<br><br><u>Incidencia závažných vaskulárnych komplikácií – následná kontrola po 30 dňoch</u><br>1. časť<br>– Bez vaskulárnych komplikácií 20/20 (100 %)<br>2. časť<br>Pseudoaneuryzma – 1/59 (1,69 %)<br><br><u>Zlyhanie ošetrovania</u><br>1. časť – 0/20 (0 %)<br>2. časť – 3/60 (5 %)<br>• 2 z dôvodu nedosiahnutia hemostázy bez použitia kompresie<br>• 1 z dôvodu závažnej vaskulárnej |

|  |  |  |  |  | komplikácie,<br>pseudoaneuryzmy |
|--|--|--|--|--|---------------------------------|
|  |  |  |  |  | <u>Pretrvávajúci výtok</u>      |
|  |  |  |  |  | 1. časť – 0/20 (0 %)            |
|  |  |  |  |  | 2. časť – 8/60 (13 %)           |
|  |  |  |  |  | <u>Hematóm</u>                  |
|  |  |  |  |  | 1. časť – 0/20 (0 %)            |
|  |  |  |  |  | 2. časť – 6/60 (10 %)           |

V rámci plánu vývoja pre FemoSeal™ VCS pred uvedením na trh boli vykonané 3 testy funkčnosti na zvieratách. v roku 2000 sa pred začatím klinických štúdií vykonala štúdia na zvieratách s cieľom posúdiť biologickú funkčnosť pomôcky FemoSeal™ VCS. Táto štúdia hodnotila schopnosť uzatváracích prvkov udržiavať fyziologickú funkciu a vyhodnotila ich rozkladanie. Po 18 mesiacoch už nebol viditeľný materiál vnútorného ani vonkajšieho disku a bol nahradený endoluminálnym fibróznym tkanivom. Na záver sa potvrdila schopnosť uzatváracieho prvku FemoSeal™ VCS zachovať fyziologickú funkciu pri použití v obehovom systéme.

V roku 2002 sa vykonala štúdia na zvieratách s cieľom posúdiť biokompatibilitu a biofunkčnosť biologicky odbúrateľného implantátu FemoSeal™ VCS, ktorý je určený na dosiahnutie hemostázy v cievnom systéme Zhrnutie: rozloženie implantátu bolo takmer dokončené do 36 týždňov a nedošlo k žiadnej významnej nežiaducej reakcii tkaniva.

Ďalšia štúdia na zvieratách v roku 2002 hodnotila biokompatibilitu a biofunkčnosť biologicky odbúrateľného implantátu FemoSeal™ VCS, ktorý je určený na dosiahnutie hemostázy v cievnom systéme. Po 5 týždňoch bola enkapsulácia disku dokončená a spozorovali sa známky rozloženia vnútorných a vonkajších diskov. Na záver sa potvrdila schopnosť implantátu zachovať fyziologickú funkciu pri použití v obehovom systéme.

V rámci plánu klinického vývoja pre pomôcku FemoSeal™ VCS vykonala spoločnosť Radi Medical System AB klinické skúšanie pred uvedením na trh. Toto klinické skúšanie nie je zverejnené ani dostupné online. Štúdia s modelom zariadenia č. 11200 sa vykonala v roku 2002-2004 v súlade s európskou normou EN 540 (Klinické skúšanie zdravotníckych pomôcok na humánne použitie) a v súlade s usmerneniami ICH Všeobecné úvahy pre klinické skúšky a Usmerneniami pre správnu klinickú prax. Podrobnosti tejto štúdie sú zdokumentované v správe EU-SE-001. Klinické skúšanie bolo zdokumentované v záverečnej správe od spoločnosti Radi Medical Systems AB, „Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures“.

Klinická štúdia bola vykonaná s prvým modelom pomôcky FemoSeal™ č. 11200 so zameraním na bezpečnosť a účinnosť implantovateľných uzatváracích komponentov. Jediný rozdiel medzi prvým modelom č. 11200 a aktuálnym modelom C11202 je francúzska veľkosť 6F a 7F a vylepšený zavádzací systém. Klinické prínosy, určené použitie, princípy fungovania a suroviny implantovateľných uzatváracích prvkov, vnútorného uzáveru a vonkajšieho uzamykacieho disku zostávajú nezmenené.

Určené použitie tejto pomôcky bolo u pacientov podstupujúcich diagnostické kardiologické alebo intervenčné kardiologické zákroky s použitím femorálnej artérie ako prístupového bodu. Cieľom tejto štúdie bolo stanoviť bezpečnosť, výkonnosť a účinnosť pomôcky FemoSeal™ VCS. Bola to prospektívna, multicentrická, jednoskupinová, otvorená štúdia s následnou kontrolou po 30 dňoch.

Primárnym koncovým ukazovateľom výkonnosti bol čas na dosiahnutie hemostázy definovaný ako neprítomnosť rýchleho krvácania. Primárnym ukazovateľom bezpečnosti bol výskyt závažných vaskulárnych komplikácií počas 30 dní. Sekundárne koncové ukazovatele zahŕňali čas do ambulácie, pomer zlyhaní liečby, výskyt nežiaducich udalostí a výkonové charakteristiky pomôcky počas zavedenia a používania.

Pacienti zahrnutí do tejto štúdie boli dospelí, schopní poskytnúť informovaný súhlas a mali aspoň jeden neporušený pedálny pulz. Pacienti boli vylúčení zo štúdie, ak sa u nich vyskytol niektorý z nasledujúcich stavov:

- Periférne cievne ochorenie v anamnéze
- Autoimunitné ochorenie
- Známe poruchy krvácania s ťažkou anémiou
- INR >1,5
- Infarkt myokardu v priebehu 72 hodín
- Nekontrolovaná hypertenzia napriek liečbe
- Obezita brániaca prístupu pomocou Seldingerovej techniky
- Prítomnosť vaskulárneho štepu alebo stentu v mieste arteriotómie
- Predchádzajúca ipsilaterálna punkcia do 3 mesiacov
- Očakávaná životnosť < 6 mesiacov

Okrem toho boli pacienti počas operácie vyšetrení a vylúčení zo štúdie, ak bolo pozorované jedno z nasledujúcich:

- Priemer lúmenu spoločnej femorálnej artérie < 5 mm
- Arteriálne vetvy do 2 cm proximálne od miesta vpichu

- Závažná stenóza do 3 cm od miesta vpichu
- Použitie primárneho zavádzacieho puzdra > 6 Fr
- Miesto vpichu je na úrovni bifurkácie femorálnej artérie alebo distálne k nej
- Viaceré femorálne punkcie
- Potvrdené alebo predpokladané prepichnutie zadnej femorálnej steny
- Veľký hematóm (2:6 cm) po dokončení zákroku
- Ťažké zavedenie primárneho puzdra pre zákrok z dôvodu torzného tkaniva alebo cievy

Táto štúdia s jedným protokolom bola vykonaná v dvoch častiach: v 1. časti bolo zaradených 20 pacientov, potom sa vykonala bezpečnostná analýza a počas 2. časti sa zaregistrovalo ďalších 60 pacientov.

V 1. časti bol stredný vek zaradených pacientov 65,9 rokov, 70,0 % pacientov bolo mužov a 95 % pacientov malo súbežne podávané lieky. v 2. časti štúdie bol stredný vek 63,8 roka, 78 % boli muži a 100 % malo súbežne podávané lieky.

Na zaradenie do štúdie spĺňali podmienky pacienti podstupujúci diagnostické (časť 1 a časť 2) alebo intervenčné (časť 2) katetrizačné zákroky na srdci. Tieto postupy boli v súlade so štandardom starostlivosti v každej z registrovaných nemocníc, po ktorej nasledovalo použitie pomôcky FemoSeal™ VCS. Údaje o pacientovi boli zhromaždené na začiatku štúdie, počas zákroku a 1 deň a 30 dní po zákroku. Výsledky sú zhrnuté v **tabuľke 1.5** a naznačujú, že systém FemoSeal™ VCS je bezpečný a účinný na použitie v tejto populácii pacientov.

**Tabuľka 1.5 Klinické výsledky hlásené v štúdiu pred uvedením na trh**

|                                                                                                       | 1. časť     | 2. časť               |
|-------------------------------------------------------------------------------------------------------|-------------|-----------------------|
| Počet pacientov                                                                                       | 20          | 60                    |
| Stredný čas do hemostázy                                                                              | 1,2 minúty  | 1,6 min <sup>a</sup>  |
| Stredný čas do ambulácie                                                                              | 72,2 minúty | 87,5 min <sup>b</sup> |
| Incidencia závažných vaskulárnych komplikácií <sup>c</sup>                                            | 0 (0 %)     | 1 (2 %)               |
| Počet pacientov s nežiaducimi udalosťami                                                              | 5 (25 %)    | 19 (32 %)             |
| Zlyhanie liečby (definované ako závažné vaskulárne komplikácie, nutnosť ručnej kompresie alebo oboje) | 0 (0 %)     | 3 (5 %)               |
| Poruchy pomôcky                                                                                       | 0 (0 %)     | 6 až (10 %)           |

<sup>a</sup> Na základe celkovej veľkosti vzorky 58, pretože 2 pacienti nedosiahli hemostázu v čase zákroku z dôvodu predchádzajúcej ipsilaterálnej punkcie. Hemostáza sa dosiahla po 7 minútach a 37 minútach u týchto pacientov.

<sup>b</sup> Na základe celkovej veľkosti vzorky 59: 1 pacient nebol zahrnutý, pretože bol umiestnený na ventilátor z dôvodu pľúcneho edému a nebol schopný ambuloval viac ako týždeň.

<sup>c</sup> Definované ako vaskulárna komplikácia vyžadujúca transfúziu krvi alebo chirurgický opravný zákrok alebo lokálna infekcia vyžadujúca podávanie antibiotík, hospitalizáciu alebo predĺženie hospitalizácie alebo odstránenie cudzích telies z miesta vpichu

V 1. časti štúdie sa nepozorovali žiadne závažné vaskulárne komplikácie. v 2. časti štúdie bola hlásená 1 závažná vaskulárna komplikácia: pseudoaneuryzma, ktorá bola hlásená do 1 dňa po zákroku. Udalosť vyžadovala kompresiu pod ultrazvukovou kontrolou a injekciu trombínu do pseudoaneuryzmy a predĺžila hospitalizáciu pacienta.

Z 5 nežiaducich udalostí hlásených v 1. časti štúdie sa vyskytla 1 nežiaduca udalosť potenciálne súvisiaca s pomôckou: nezávažná udalosť rýchleho krvácania 1. deň po zákroku. z 19 nežiaducich udalostí hlásených v 2. časti štúdie sa pozorovali 3 nežiaduce udalosti hematómu súvisiace s pomôckou a 6 nezávažných udalostí potenciálne súvisiacich s pomôckou vrátane 3 hlásení pretrvávajúceho výtoku, 2 hematómov a 1 bolesti nohy po cvičení.

V 2. časti bola u 3 pacientov liečba považovaná za zlyhanú: u 2 z dôvodu nedosiahnutia hemostázy bez použitia kompresie a u 1 z dôvodu závažnej vaskulárnej komplikácie (pseudoaneuryzma). v 1. časti štúdie sa nevyskytli žiadne zlyhania liečby.

Zo šiestich porúch pomôcky v 2. časti štúdie tri nemali vplyv na zákrok, jedna bola priradená k chybe používateľa, jedna bola presakovanie závädzača a jedna predstavovala zlomený spoj filamentu. Posledné dva problémy boli riešené aktualizáciami implementovanými v modeli C11202.

2. časť klinickej štúdie pred uvedením na trh nehlásila výsledky následnej kontroly po 6 mesiacoch z dôvodu nesplnenia požiadaviek pacienta. Výsledky po 30 dňoch v klinickej štúdii pred uvedením na trh (EU-SE-001), čo je v súlade s obdobím následných kontrol v klinickej literatúre, dokazujú, že pomôcka FemoSeal™ VCS je bezpečná a účinná.

## 1.4.2 Súhrn údajov z klinických štúdií po uvedení na trh

V **tabuľke 1.6** nižšie sú popísané 4 ukončené klinické štúdie po uvedení na trh. Tieto klinické skúšania nie sú zverejnené ani dostupné online.

**Tabuľka 1.6 Klinické štúdie po uvedení na trh**

| Dokončené klinické štúdie po uvedení na trh                                                    |                                                              |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|------------------------------------------------------------------------------------------------|--------------------------------------------------------------|--------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|----|-----|----------|-------|----------|-----------|----|-----------|-----------|-------------------------|----------|--------------------|------------|---------------------|-----------|-------------------|---------|-----------------------|----------|--------------------------------|----------|----------------------|-----------|--------------------------|-----------|-----------------------------------|----------|----------------------|--------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Názov štúdie                                                                                   | Rok / CI                                                     | Typ štúdie                                                         | Ciele                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Medzníky                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Potenciálne kritériá akceptácie                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)<br>User Acceptability of New Packaging (SIS) (2006) | 2006<br><br>RADI                                             | Štúdia po uvedení na trh, akceptovanie nového balenia používateľom | Štúdia po uvedení na trh vykonaná na základe aktualizácie modelu FemoSeal Vascular® Closure System č. 11202, ktorý má upravený zavádzací systém v porovnaní s prvým modelom č. 11200, na zdokumentovanie funkčnosti.<br><br>Cieľom štúdie bolo získať spätnú väzbu o revidovanom návode na použitie, školiacom programe pre lekárov a zdravotné sestry, overiť hodnotenia vykonané v analýze rizík a poskytnúť informácie s cieľom vylepšenia kvality výrobkov. | 100 pacientov <ul style="list-style-type: none"><li>63 mužov/37 žien</li><li>Priemerný vek 68 rokov pre ženy, 65 rokov pre mužov</li></ul> 2 nemocnice vo Švédsku, 6 lekárov<br><br>112 pomôcok<br><br>Údaje zaznamenané vo formulároch záznamov o pacientovi (CRF)<br><br>Plánovaný čas pozorovania – 30 minút od času aplikácie                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Výsledky<br><br>1. Ilustrácie/pokyny v návode na použitie sa považujú za informatívne a primerané<br><br>2. Okamžitá hemostáza (91/100) |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)              | Dr. Nicolas Moes<br>Innsbruck Medical University,<br>Rakúsko | Potvrdzujúce posudzovanie po uvedení na trh                        | Cieľom tejto štúdie bolo vyhodnotiť bezpečnosť a výkonnosť pomôcky FemoSeal® používanej počas bežných klinických postupov u pacientov, ktorí podstupujú diagnostickú katetrizáciu srdca alebo perkutánnu intervenčnú srdcový zákrok s použitím 7F puzdra.                                                                                                                                                                                                       | 50 po sebe nasledujúcich pacientov<br><br>Indikácie – diagnostická alebo invazívna katetrizácia srdca zo spoločnej femorálnej artérie<br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                       | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Primárne koncové ukazovatele <ul style="list-style-type: none"><li>Primárny koncový ukazovateľ účinnosti – TTH (čas do hemostázy) s výtokom alebo bez, ale bez dodatočnej kompresie, ručnej alebo mechanickej.</li><li>Bezpečnostný koncový ukazovateľ – výskyt nežiaducich udalostí – menšie a závažné vaskulárne komplikácie a všetky ostatné nežiaduce udalosti – vážne a nezávažné počas trvania štúdie (t. j. až do prepustenia pacienta).</li></ul> Výsledky <ul style="list-style-type: none"><li>Stredný čas do hemostázy</li><li>Diagnostika – 56,6 ± 29 sekúnd</li><li>Intervencia 59,9 ± 16,2 sekundy</li><li>Všetci pacienti 57,8 ± 26,3</li></ul> |
| n                                                                                              | 50                                                           |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| men                                                                                            | 35 (70%)                                                     |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| women                                                                                          | 15 (30%)                                                     |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| PCI cases                                                                                      | 15                                                           |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| age (yrs)                                                                                      | 62.8±11.1                                                    |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| body mass index (kg/m²)                                                                        | 25.4±6.7                                                     |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| systolic BP (mmHg)                                                                             | 131.2±20.9                                                   |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| diastolic BP (mmHg)                                                                            | 77.9±10.6                                                    |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| diabetes mellitus                                                                              | 9 (18%)                                                      |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| arterial hypertension                                                                          | 34 (68%)                                                     |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| previous coronary intervention                                                                 | 13 (26%)                                                     |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| preprocedure aspirin                                                                           | 50 (100%)                                                    |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| preprocedure clopidogrel                                                                       | 50 (100%)                                                    |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Procedural unfractionated heparin                                                              | 15 (30%)                                                     |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Procedural abciximab                                                                           | 2 (4%)                                                       |                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                         |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |



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|                                                                                                                                 |                                 |                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                | <ul style="list-style-type: none"> <li>Všetci pacienti mohli být bez problémů po 4 hodinách pokoja na lůžku ambulantů.</li> </ul> <p>Výsledky bezpečnosti</p> <ul style="list-style-type: none"> <li>49/50 (98 %) bez vaskulárních komplikací, do prepustenia z nemocnice</li> <li>Stredný čas do prepustenia 2,6 dňa</li> <li>1/50 (2 %) drobné krvácanie nasledujúci deň po bezproblémovej ambulácii v deň angiografie</li> </ul>                                                                                                                                                                             |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | 2009 RADI                       | Štúdia po uvedení na trh                                          | <p>Štúdia by mala priniesť informácie o tom, či zákazníci/používatelia vnímali nejaké problémy s novým balením, najmä s nesterilnou vonkajšou stranou vrečka Tuvek/PET-PE.</p> <p>Štúdia by mala poskytnúť aj informácie o tom, či ošetrojúci lekár vníma rozdiely v krokoch aplikácie/zavedenia pomôcky v porovnaní s predtým používanými pomôckami.</p> <p>Štúdia by mala tiež poskytnúť informácie o ďalších potrebách na zlepšenie kvality výroby.</p> | <p>25 pomôcok</p> <p>4 nemocnice vo Švédsku</p> <p>16/25 (64 %) pacientov boli pacienti s PCI s intenzívnou antikoagulačnou liečbou</p>                                                                                                                                                                        | <p>Výsledky</p> <ol style="list-style-type: none"> <li>Problémy súvisiace s balením – 21 z 25 (84 %) aplikácií bolo úspešných; 4 z 25 (16 %) bolo neúspešných (1 – testovanie nového zavádzača, 1 vnútorný disk prešiel cez arteriotómiu v kroku vytahovania, tlačidlo vyskočilo nazad a vonkajší disk bol umiestnený do kanála tkaniva v reze, 2 okamžitá hemostáza sa nedosiahla napriek absencii problémov s nasadením.)</li> <li>Okamžitá hemostáza 19/25 (76 %) pacientov</li> <li>Krvácanie 11/25 (44 %) – 9/25 (36 %) výtok/krvácanie, hematómy 2/25 (8 %)</li> </ol> <p>Celková miera udalostí 19 %</p> |
| The FemoSeal Vascular Closure System (VCS) Registry: a Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022) | 2022/Terumo Medical Corporation | Prospektívna, multicentrická, observačná štúdia po uvedení na trh | Cieľom tejto štúdie je ďalej preukázať bezpečnosť a účinnosť pomôcky FemoSeal™ VCS pri dosahovaní hemostázy miest prístupu do spoločnej femorálnej artérie (CFA) u osôb v reálnej situácii, ktorí podstupujú perkutánne endovaskulárne zákroky                                                                                                                                                                                                             | <ul style="list-style-type: none"> <li>Sledovanie pacienta po 30 dňoch (<math>\pm</math> 7 dní) návštevou nemocnice alebo telefonickým hovorom.</li> <li>Prihlásenie: december 2021 až júl 2022.</li> <li>230 zaradených osôb podstupujúcich diagnostické alebo intervenčné endovaskulárne zákroky,</li> </ul> | <ul style="list-style-type: none"> <li><b>Demografické charakteristiky/komorbidity:</b> <ul style="list-style-type: none"> <li>- Pohlavie 161 mužov (70 %)/69 žien 69 (30 %).</li> <li>- Priemerný vek: 70 <math>\pm</math> 12.</li> <li>- BMI: 26,1 <math>\pm</math> 4,95 kg/m<sup>2</sup>.</li> <li>- Hypertenzia: 160 pacientov (69,6 %).</li> <li>- Dyslipidémia: 128 (55,7 %).</li> <li>- Ochorenie koronárnych artérií: 42 (18,3 %).</li> </ul> </li> </ul>                                                                                                                                               |

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|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  | <p>pri ktorých sa používa FemoSeal™.</p> <p>3 európske pracoviská:<br/>Francúzsko (92 pacientov),<br/>Nemecko (38 pacientov),<br/>Belgicko (100 pacientov).</p> | <ul style="list-style-type: none"> <li>- Aktuálny fajčiar: 86 (37,6 %).</li> <li>- Fajčiar v minulosti: 66 (28,8 %).</li> <li>- Koronárne ochorenie srdca: 34 (14 %).</li> <li>- Predchádzajúci infarkt myokardu: 18 (7,8 %).</li> <li>- Revaskularizácia periférnej artérie: 12 (5,2 %) karotída 83 (37,5 %) a artéria dolnej končatiny.</li> <li>- Protidoštičková liečba (na začiatku štúdie): 211 (91,7 %) vrátane 21 (9,1 %) duálnej protidoštičkovej liečby (DAPT).</li> <li>- Perorálna antikoagulácia: 40 (17,4 %) pacientov.</li> <li>• <b>Charakteristika zákroku:</b> <ul style="list-style-type: none"> <li>- Miesto: lôžková klinika 162 prípadov (70,4 %), ambulantná klinika 68 prípadov (29,6 %).</li> <li>- Prevládajúca indikácia: kľaudikácia 147 prípadov (63,9 %).</li> <li>- Prístup: 35 antegrádne (15,3 %), 194 retrográdne (84,7 %).</li> </ul> </li> <li>• <b>Primárne koncové ukazovatele:</b> <ul style="list-style-type: none"> <li>- Kombinovaný koncový ukazovateľ bezpečnosti (stav bez závažných komplikácií končatiny v mieste prístupu do 6 hodín po zákroku) a účinnosti (úspešná hemostáza v mieste vpichu) bol dosiahnutý u 215/226 (95,1 %) [95 % IS: 91,46; 97,55] pacientov v úplnom súbore analýzy a 215/230 (93,5 %) [95 % IS 89,47; 96,30] v súbore liečenom pomôckou FemoSeal™.</li> <li>- Koncový ukazovateľ účinnosti bol dosiahnutý u 219/226 (96,9 %) IS [93,7; 98,7] pacientov.</li> </ul> </li> </ul> |
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|--|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <p>- Koncový ukazovateľ bezpečnosti bol dosiahnutý u 220/230 (95,2 %) [95 % IS: 92,15; 97,90] pacientov.</p> <p>• <b>Sekundárne koncové ukazovatele:</b></p> <p>- Stav bez menších komplikácií v mieste prístupu počas šiestich hodín po zákroku bol dosiahnutý u 225/230 (97,8 %) [95 % IS: 95,00; 99,29].</p> <p>- Stav bez závažných a menších komplikácií v mieste prístupu od šiestich hodín do 30 dní po zákroku bol dosiahnutý u 219/230 (95,2 %) pacientov [95 % IS: 91,60; 97,59].</p> <p>- Medián času do dosiahnutia hemostázy s pomocou FemoSeal™ VCD: 0,42 (0,25; 0,50) minút.</p> <p>- Medián času do ambulácie: 5,00 (4,54; 5,50) minút.</p> <p>- Medián dĺžky hospitalizácie: 23,98 (22,72; 25,00) hodín.</p> <p>- Použitelnosť pomôcky FemoSeal™ VCS: „ľahké“ alebo „veľmi ľahké“ zavedenie v 98,7 % prípadov („ľahké“ zavedenie v 21 prípadoch (9,2 %), „veľmi ľahké“ zavedenie v 205 prípadoch (89,5 %)) so žiadnym alebo nízkym odporom pri zavedení v 226 prípadoch (98,3 %).</p> <p>152/230 (66,1 %) pacientov liečených pomocou vodiaceho drôtu zahrnutého v súprave FemoSeal™ (GW 0,038") a odporúčaného na použitie so súpravou FemoSeal™ bez hlásených nedostatkov pomôcky alebo nežiaducich udalostí.</p> |
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Štúdia z roku 2006 bola vykonaná na potvrdenie bezpečnosti a účinnosti aktuálnej pomôcky so zlepšeným zavádzacím systémom a na získanie spätnej väzby v súvislosti s návodom na použitie pomôcky FemoSeal™ VCS a školiacim programom. Štúdia zahŕňala 100 pacientov a primárnym koncovým ukazovateľom bolo, či sa dosiahla hemostáza, alebo či boli potrebné ďalšie manuálne alebo mechanické kompresie. Záverom tejto štúdie bolo, že použitie pomôcky FemoSeal™ VCS bolo úspešné vo väčšine prípadov (91 % dosiahlo okamžitú hemostázu).

Štúdia z roku 2008 zahŕňala 50 pacientov na posúdenie bezpečnosti a výkonnosti pomôcky FemoSeal™ VCS pri použití počas bežnej klinickej praxe u pacientov podstupujúcich katetrizáciu srdca s puzdrom veľkosti 7 Fr. Primárnym koncovým ukazovateľom štúdie bolo zhromaždiť údaje o čase do hemostázy a čase do ambulácie bez dodatočnej kompresie, ručnej alebo mechanickej. Výsledkom štúdie bolo, že stredný čas na dosiahnutie hemostázy bol 57,8 sekundy a všetci pacienti po 4 hodinách pokoja na lôžku boli ambulovaní.

Štúdia z roku 2009 mala za cieľ vyhodnotiť nové balenie FemoSeal™ VCS. Do štúdie bol zaradených 25 pacientov. Primárnym koncovým ukazovateľom bolo, či používateľ mal s obalom nejaké problémy. Používatelia nezaregistrovali žiadne problémy týkajúce sa nového balenia pomôcky FemoSeal™ VCS. Táto štúdia získala tiež údaje o čase do hemostázy.

Cieľom štúdie z roku 2022 bolo zozbierať údaje o bezpečnosti a účinnosti pomôcky FemoSeal™ VCS pri dosahovaní hemostázy miest prístupu do spoločnej femorálnej artérie (CFA) u osôb v reálnej situácii, ktorí podstupovali perkutánne endovaskulárne zákroky. Do štúdie bol zaradených 230 pacientov. Primárne koncové ukazovatele pre register sú úspešnosť zákroku (t. j. úspešná hemostáza v mieste vpichu) a zníženie závažných komplikácií (napr. poranenie ciev, krvácanie v mieste prístupu, infekcia v mieste prístupu, opakovaná manuálna kompresia a nová ipsilaterálna akútna ischémia nohy súvisiaca s miestom prístupu). Štúdia dospela k záveru, že pomôcka FemoSeal™ VCS funguje dobre v reálnom prostredí, vytvára účinnú hemostázu a má nízku mieru komplikácií v mieste prístupu u pacientov podstupujúcich periférne endovaskulárne zákroky. Preukazuje dobrú výkonnosť s krátkym časom do dosiahnutia hemostázy a dobrou spätnou väzbou od používateľa, vďaka čomu je systém FemoSeal™ VCS cenná pomôcka na uzavretie femorálneho prístupu.

### **1.4.3 Súhrn údajov z klinického sledovania po uvedení na trh**

#### **1.4.3.1 Dokončené klinické sledovanie po uvedení na trh**

Súhrn dokončených činností klinického sledovania po uvedení na trh je uvedený v **tabuľke 1.7** nižšie.

**Tabuľka 1.7. Činnosti klinického sledovania po uvedení na trh**

| Dokončené činnosti klinického sledovania po uvedení na trh                |             |                                                               |                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                    | Potenciálne kritériá akceptácie                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|---------------------------------------------------------------------------|-------------|---------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Názov činnosti                                                            | Rok/Spol.   | Typ štúdie                                                    | Ciele                                                                                                                                                                                                  | Medzníky                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021<br>TMC | Klinický prieskum po uvedení na trh – vysokokvalitný prieskum | Prieskum po uvedení na trh na zhromaždenie prospektívnej spätnej väzby o používaní pomôcky na uzatváranie ciev FemoSeal™ Vascular Closure Device distribuovanej na trhoch Európskej únie.              | <ul style="list-style-type: none"> <li>120 prípadov</li> <li>8 rôznych lekárov s &gt; 5 rokmi skúseností</li> <li>Viacere krajiny v Európe</li> </ul>                                                                                                                                                                              | <b>Hodnotenia pomôcky na stupnici 1-5 – vyhlásenia z prieskumu</b> <ul style="list-style-type: none"> <li>Kritériá prijatia <ul style="list-style-type: none"> <li>Dosiahnuté hodnotenia 3 - 5 sa považujú za priaznivé</li> <li>Všetky vyhlásenia majú mať <math>\geq 80\%</math> pozitívnu spätnú väzbu</li> </ul> </li> <li>Výsledky <ul style="list-style-type: none"> <li>Žiadne vyhlásenie z prieskumov nezískalo &gt; 20 % nepriaznivých odpovedí</li> <li>Neboli podané žiadne sťažnosti na pomôcku</li> </ul> </li> </ul> |
| 20210298 – 0,035" and 0038" Guidewire Clinical Survey Report (2021)       | 2021<br>TMC | Klinický prieskum po uvedení na trh – vysokokvalitný prieskum | Prieskum po uvedení na trh na zhromaždenie prospektívnej spätnej väzby o používaní vodiaceho drôtu s priemerom 0,035" dodávaného s pomôckou Angio-Seal™ VIP Vascular Closure Device (VCD) veľkosti 6Fr | <ul style="list-style-type: none"> <li>Prieskumy pre 0,035" drôt <ul style="list-style-type: none"> <li>106 dotazníkov</li> <li>64 lekárov</li> </ul> </li> <li>Prieskumy pre 0,038" drôt <ul style="list-style-type: none"> <li>109 dotazníkov</li> <li>55 lekárov</li> </ul> </li> <li>12 retrospektívnych dotazníkov</li> </ul> | <b>Hodnotenia pomôcky na stupnici 1-5 – vyhlásenia z prieskumu</b> <ul style="list-style-type: none"> <li>Kritériá prijatia <ul style="list-style-type: none"> <li>Dosiahnuté hodnotenia 3 - 5 sa považujú za priaznivé</li> <li>Všetky vyhlásenia majú mať <math>\geq 80\%</math> pozitívnu spätnú väzbu</li> </ul> </li> <li>Výsledky</li> </ul>                                                                                                                                                                                 |

| Dokončené činnosti klinického sledovania po uvedení na trh                                                                      |                     |                                                               |                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|---------------------------------------------------------------------------------------------------------------------------------|---------------------|---------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                 |                     |                                                               | a s priemerom 0,038" dodávaného s pomôckou Angio-Seal™ VIP VCD veľkosti 8Fr a systémom FemoSeal Vascular Closure System distribuovaným na trhoch Európskej únie. |                                                                                                                                                                                                                                                                                                                           | <ul style="list-style-type: none"> <li>○ Všetky vodiace drôty dostali prijateľné hodnotenia</li> <li>○ Neboli podané žiadne sťažnosti na pomôcku</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024<br>TMC/TE | Klinický prieskum po uvedení na trh – vysokokvalitný prieskum | Prospektívne zhromažďovanie spätnej väzby súvisiacej s používaním pomôcky FemoSeal VCS s vodiacími drôťmi distribuovanými na trhu EÚ.                            | <ul style="list-style-type: none"> <li>• 126 prieskumov</li> <li>• 7 pracovísk</li> <li>• 5 krajín</li> <li>• 14. novembra 2023 – 11. júna 2024</li> <li>• Špecializácia lekára: <ul style="list-style-type: none"> <li>○ Cievna chirurgia</li> <li>○ Intervenčná rádiológia</li> <li>○ Angiológia</li> </ul> </li> </ul> | <b>Hodnotenia pomôcky na stupnici do 5 – vyhlásenia z prieskumu</b> <ul style="list-style-type: none"> <li>• Kritériá prijatia <ul style="list-style-type: none"> <li>○ Dosiahnuté hodnotenia 3 - 5 sa považujú za priaznivé</li> <li>○ Všetky vyhlásenia majú mať <math>\geq 80\%</math> pozitívnu spätnú väzbu</li> <li>○ Ak sa v tomto prieskume vyskytnú nežiaduce udalosti, mali by to byť tie, ktoré predpokladá manažment rizík.</li> </ul> </li> <li>• Demografické informácie pacientov <ul style="list-style-type: none"> <li>○ Ženy: 29,4 % (37/126)</li> <li>○ Muži: 69,8 % (88/126)</li> <li>○ Pohlavie nie je uvedené: 0,8 % (1/126)</li> </ul> </li> </ul> |

| Dokončené činnosti klinického sledovania po uvedení na trh |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|------------------------------------------------------------|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                            |  |  |  |  | <ul style="list-style-type: none"> <li>○ Vek<br/>&gt; 75 rokov:<br/>31,7 %</li> <li>• Výsledky <ul style="list-style-type: none"> <li>○ Vodiaci drôt<br/>dodávaný<br/>s pomôckou<br/>FemoSeal™<br/>VCS: 101/126<br/>(80,2 %).</li> <li>○ Trvanie<br/>zároku<br/>(minúty): 63,4<br/>(36,6) (priemer<br/>(SD)); 57,0<br/>(36,0 – 81,0)<br/>(medián<br/>(IQR))</li> <li>○ Všetky<br/>hodnotenia<br/>výkonnosti<br/>pomôcky<br/>FemoSeal™<br/>VCS boli<br/>priaznivé.</li> <li>○ Všetky<br/>hodnotenia<br/>vodiaceho<br/>drôtu<br/>dodaného<br/>s pomôckou<br/>FemoSeal™<br/>VCS boli<br/>priaznivé.</li> <li>○ Jedna<br/>nežiaduca<br/>udalosť<br/>(0,8 %): diský<br/>pomôcky<br/>FemoSeal™<br/>VCS neboli<br/>správne<br/>zarovnané<br/>pravdepodobne<br/>z dôvodu<br/>použitia<br/>tuhého<br/>vodiaceho<br/>drôtu (Boston</li> </ul> </li> </ul> |

| Dokončené činnosti klinického sledovania po uvedení na trh |  |  |  |  |                                                                                                                                         |
|------------------------------------------------------------|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------|
|                                                            |  |  |  |  | Scientific<br>Amplatz Super<br>Stiff, 75 cm,<br>0,035 palca),<br>čo vyžadovalo<br>manuálnu<br>kompresiu na<br>dosiahnutie<br>hemostázy. |

Spoločnosť Terumo Medical Corporation vykonala tri vysokokvalitné prieskumy používateľov z radov lekárov počas aktuálneho vykazovaného obdobia (1. september 2019 - 31. august 2024).

Klinické prieskumy FemoSeal™ zhromažďovali proaktívne klinické údaje týkajúce sa bezpečnosti a výkonnosti pomôcky FemoSeal™ VCS počas klinického používania. Prieskum obsahoval otázky zamerané celkovo na pomôcku a súvisiace príslušenstvo vrátane vodiaceho drôtu s rozmerom 0,038" a ich priamych interakcií. Klinické prieskumy týkajúce sa vodiacich drôtov zhromažďovali proaktívne klinické údaje vo vzťahu k bezpečnosti a výkonnosti počas klinického používania vodiaceho drôtu s rozmerom 0,038" dodávaného spolu s pomôckou FemoSeal™ VCS. Otázky prieskumu sú zamerané špecificky na všeobecné použitie vodiaceho drôtu od zavedenia cez procedurálny zavádzáč do vaskulatúry až po odstránenie drôtu.

Pomôcka FemoSeal™ VCS a vodiaci drôt 0,038" dodaný s pomôckou získali na základe vyhodnotenia pripomienok získaných z vysokokvalitných klinických prieskumov všetky prijateľné hodnotenia a šesť (6) sťažností bolo zaznamenaných pre pomôcku a deväť (9) podnetov týkajúcich sa vodiaceho drôtu. Sťažnosti boli posúdené pre pomôcku FemoSeal a vodiaci drôt a boli vyhodnotené ako súčasť procesu spoločnosti Terumo sledovania po uvedení na trh. Neboli identifikované žiadne nové riziká ani úrovne rizika.

V roku 2024 bol v rámci aktivít PMCF vykonaný prieskum používateľov z radov lekárov. Výsledky prieskumu preukázali, že hodnotenie výkonnosti a bezpečnosti pomôcky FemoSeal™ VCS boli celkovo veľmi priaznivé. Bola preukázaná aj kompatibilita iných vodiacich drôtov ako je štandardný drôt dodávaný s pomôckou FemoSeal™ VCS.

#### 1.4.3.2 Prebiehajúce/plánované klinické sledovanie po uvedení na trh

TMC má jedno prebiehajúce/plánované klinické sledovanie po uvedení na trh. Klinický prieskum bude ukončený na prospektívne zozbieranie spätnej väzby týkajúcej sa používania vodiaceho drôtu s pomôckou FemoSeal VCS distribuovanou na trhu v EÚ. Tento prieskum vyplnia lekári, aby sa zistilo, ktoré vodiace drôty sa používajú počas zákroku. Účel prieskumu je



zamerať sa na medzeru identifikovaných ako nedostatok literatúry a komentárov externých recenzentov o kompatibilitu pomlcky FemoSeal™ VCS s použitím iných vodiacich drôtov od iných značiek ako Terumo. Spätná väzba zahŕňa technické výsledky, klinickú výkonnosť a bezpečnosť týkajúce sa výkonnosti pomôcky s rôznymi vodiacími drôťmi.

#### 1.4.4 Súhrn údajov zo systematického prehľadu literatúry

Spoločnosť Terumo Medical Corporation vykonáva systematický prehľad literatúry s cieľom zhromažďovať a vyhodnocovať údaje o klinickej bezpečnosti a výkone z publikovaných štúdií o pomôcke FemoSeal™ VCS a/alebo podobných pomôckach. Cieľom každoročného vyhľadávania v publikovanej literatúre je identifikovať doteraz neznáme vedľajšie účinky, sledovať známe vedľajšie účinky, identifikovať nové riziká a identifikovať možné systematické nesprávne používanie alebo používanie mimo indikácie pomôcky FemoSeal™ VCS.

Najnovší systematický prehľad literatúry, ktorý zahŕňal obdobie od 1. septembra 2019 do 31. augusta 2024, identifikoval 29 publikovaných štúdií, v ktorých boli klinické údaje o bezpečnosti a výkonnosti pomôcky FemoSeal™ VCS. v 23 odkazoch sa hlásilo použitie pomôcky FemoSeal™ VCS v schválenej indikácii a použitie mimo schválenej indikácie sa hlásilo v 9 štúdiách. Vo všeobecnosti prehľad literatúry o štúdiách zameraných na špecifické používanie pomôcky FemoSeal™ VCS predstavuje skúmanú populáciu, ktorá je reprezentatívna pre pacientov v EÚ podstupujúcich perkutánne cievne katetrizačné zákroky. v **časti 3** nájdete zoznam 23 recenzovaných publikácií týkajúcich sa schválených indikácií.

Klinický výkon bol hodnotený podľa nasledujúcich ukazovateľov:

- Čas do dosiahnutia hemostázy je pri perkutánnom uzavretí spoločnej femorálnej artérie kratší alebo porovnateľný so súčasným stavom technológií.
- Čas do ambulácie je pri perkutánnom uzavretí spoločnej femorálnej artérie kratší alebo porovnateľný so súčasným stavom technológií.
- Miera pooperačných komplikácií je porovnateľná alebo nižšia ako pri aktuálnej štandardnej starostlivosti.

Na základe týchto klinických meraní výkonnosti údaje v tejto literatúre ukázali, že FemoSeal™ VCS sa môže úspešne použiť pri uzatváraní femorálnej arteriálnej punkcie (arteriotómie) u pacientov, ktorí podstúpili perkutánnu katetrizáciu pomocou 7 Fr alebo menšieho procedurálneho puzdra. Úplná hemostáza sa dosiahla u väčšiny pacientov (79,65 – 100 %) a bola spojená s mediánom času do dosiahnutia hemostázy 0,5 minúty a s priemerným časom do prepustenia z nemocnice 3 dni. 69,2 – 86,7 % pacientov bolo schopných pohybovať sa 5 hodín po uzavretí s priemerným pooperačným pokojom na lôžku 349 minút. Zlyhanie pomôcky FemoSeal™ VCS sa pozorovalo v 3,68 – 4 % prípadov a dodatočná manuálna kompresia bola potrebná v 0,9 – 4,4 % zákrokov.

Klinická bezpečnosť bola hodnotená nežiaducimi udalosťami, medzi ktoré okrem iných patria:

- Krvácanie
- Hematóm
- Pseudoaneuryzma
- Podliatina
- Arteriovenózna fistula
- Infekcia
- Smrť

V prípade každej z týchto nežiaducich udalostí bola miera výskytu hlásená pre pomôcku FemoSeal™ VCS v zahrnutých štúdiách nižšia alebo porovnateľná s mierami pre manuálnu kompresiu hlásenými v minulosti a inými pomôckami na uzatváranie ciev.

Na základe preskúmania 10 správ o prípade neboli zistené žiadne nežiaduce udalosti, keďže neboli identifikované žiadne nové, neočakávané, rozvíjajúce sa ani neprijateľné riziká.

Celková účinnosť používania pomôcky FemoSeal™ VCS počas diagnostickej angiografie alebo intervenčných chirurgických zákrokov závisí od viacerých faktorov, ako sú: pohlavie, vek, anatómia pacienta, komorbidity, anatomické umiestnenie miesta vpichu, skúsenosti chirurga, metóda zavedenia VCD, pooperačná starostlivosť, atď. Okrem technického úspechu vrátane dosiahnutia hemostázy má pomôcka FemoSeal™ VCS klinické prínosy vo vzťahu k uzavretiu ciev po femorálnej arteriálnej punkcii, ako je skrátenie času do dosiahnutia hemostázy, skrátenie času do ambulácie. Výsledky výkonnosti pre pomôcku FemoSeal™ VCS sú konzistentné s výsledkami, ktoré sa očakávajú pre tento typ pomôcky pri použití na určený účel. Niektoré z referencií zistených počas aktuálneho vyhľadávacieho obdobia ukázali použitie predmetnej pomôcky na inom anatomickom mieste ako na spoločnej femorálnej artérii a na uzavretie arteriotómií > 7Fr, čo sa považuje za použitie mimo schválenej indikácie.

Počas prieskumu sa nezistili žiadne neznáme vedľajšie účinky, rozvíjajúce sa riziká ani možné systematické nesprávne používanie pomôcky. Ak sa však pomôcka FemoSeal™ VCS používa opatrne vyškolenými lekármi, zdravotnícka pomôcka je užitočnou a potrebnou klinickou pomôckou. Celkovo cieľová liečba, a teda pomôcka FemoSeal™ VCS, rieši klinickú potrebu, ktorá v súčasnosti existuje pri liečbe komplikácií súvisiacich s cievnyim prístupom.

Celkovo údaje v tomto prehľade literatúry neidentifikovali žiadne predtým neznáme problémy s výkonnosťou alebo bezpečnosťou v klinickom prostredí alebo nežiaduce účinky, ktoré sa vyskytli vo vyššej miere, ako sa predpokladalo/akceptovalo. z tohto dôvodu možno na základe tohto prehľadu literatúry dospieť k záveru, že pomôcka FemoSeal™ VCS používaná na vytvorenie kompresie na dosiahnutie hemostázy pri arteriotómii po perkutánnej katetrizácii bude naďalej fungovať podľa očakávaní a nespája sa so závažnými bezpečnostnými udalosťami.

### 1.4.5 Súhrn údajov z dohľadu po uvedení na trh

Je zavedený proaktívny systém dohľadu po uvedení na trh (Post-Market Surveillance, PMS) a každý mesiac sa vykonáva preskúmanie všetkých sťažností v súlade s internými výrobnými postupmi. Údaje o sťažnostiach sa analyzovali v období od 1. septembra 2019 do 31. augusta 2024. Celkovo bolo k dispozícii 28 správ z dohľadu nad zdravotníckou pomôckou (Medical Device Vigilance, MDV) a 476 hlásení o sťažnostiach zákazníkov podaných výrobcovi. z 28 správ MDV 27 súviselo s nežiaducimi udalosťami a jedna s poruchou funkcie pomôcky. Počas vykazovaného obdobia došlo k dvom úmrtiam, ale žiadne z hlásených úmrtí nebolo považované za súvisiace s predmetnou pomôckou. Spomedzi 476 sťažností podaných výrobcovi boli najčastejšími dôvodmi sťažností ťažkosti so zavedením pomôcky (146 udalostí, miera výskytu 0,0142 %). Udalosti režimu poruchy pri vyťahovaní je druhý najčastejší sa vyskytujúci dôvod s mierou 0,0126 % (130 udalostí).

Cievny uzatvárací systém FemoSeal Vascular Closure System bol predaný viac ako 1 030 136-krát na celom svete a 827 843-krát v Európskom hospodárskom priestore. Vypočítaná frekvencia sťažností na základe globálneho predaja je 0,046 %. Celková miera sťažností zákazníkov je veľmi nízka. Neboli zistené žiadne nové riziká, ktoré nie sú zahrnuté v návode na použitie a v dokumentácii o rizikách.

Frekvencia výskytu nežiaducich vedľajších účinkov je uvedená v **tabuľke 1.2**. Neboli identifikované žiadne nové neočakávané, rozvíjajúce sa ani neprijateľné riziká. Nevyskytlo sa žiadne významné zvýšenie frekvencie alebo závažnosti známych nežiaducich vedľajších účinkov.

### 1.4.6 Celkový súhrn parametrov klinického výkonu a bezpečnosti

Systém FemoSeal™ VCS je indikovaný na použitie pri uzatvorení bežnej femorálnej arteriálnej punkcie (arteriotómie) u pacientov, ktorí podstúpili perkutánnu katetrizáciu pomocou 7F (2,33 mm) alebo menšieho procedurálneho zavádzača. Toto klinické hodnotenie je založené na komplexnej analýze dostupných klinických údajov pred uvedením a po uvedení na trh a literatúry, ktoré sú relevantné pre určené použitie pomôcky FemoSeal™ VCS.

Bolo vykonané komplexné preskúmanie publikovanej literatúry za obdobie od 1. septembra 2019 do 31. augusta 2024. Súbor dôkazov zahŕňal 29 štúdií pre pomôcku FemoSeal™ VCS. Dôkazmi uvedenými v klinickom hodnotení sa dospelo k záveru, že pri indikovanom použití je predmetná pomôcka bezpečná a účinná a všetky riziká alebo nežiaduce vedľajšie účinky, ktoré môžu byť spojené s pomôckou za normálnych podmienok používania, predstavujú prijateľné riziká pri zvážení oproti prínosom pre pacienta. Výsledky výkonu pre predmetné pomôcky sú konzistentné s tými, ktoré sa očakávajú pre tento typ pomôcky pri použití na určený účel.

Medzi potenciálne nežiaduce vedľajšie účinky spojené s použitím pomôcky FemoSeal™ VCS patria nežiaduce udalosti bežne hlásené pri alternatívnych spôsoboch uzáveru arteriotómie, napr.

krvácenie a hematóm. Celkovo sú miery výskytu nežiaducich udalostí hlásených pri použití pomôcky FemoSeal™ VCS podobné mieram hláseným pri manuálnej kompresii a pri použití podobných pomôcok na uzatváranie ciev. Konkrétne v prípade krvácania a hematómu sú hlásené miery pre pomôcku FemoSeal™ VCS nižšie ako hlásené miery pre podobné pomôcky na uzatváranie ciev. Každá z hlásených nežiaducich udalostí z publikovanej literatúry aj zo sledovania po uvedení pomôcky na trh bola už v minulosti identifikovaná (pozri **časť 1.3**).

Existujúce údaje týkajúce sa klinickej bezpečnosti a výkonnosti pomôcky FemoSeal™ VCS naznačujú, že prínosy pre pacientov z používania pomôcky na uzatváranie ciev prevažujú nad možnými rizikami, ak sa používa v súlade s návodom na používanie.

Ako je uvedené v predchádzajúcich častiach, údaje uvádzané pre pomôcku FemoSeal™ VCS preukazujú súlad medzi údajmi o hodnotenej pomôcke (napr. používanie pomôcky, výsledky bezpečnosti, klinická výkonnosť a klinické prínosy), identifikovanými ekvivalentnými pomôckami a údajmi o podobných pomôckach uvedených v zozname Najnovší stav technológií.

Krížovou analýzou údajov o bezpečnosti sa nezistili žiadne rozdiely medzi:

- Údajmi uvedenými v zozname Najnovší stav technológií
- Údajmi špecifickými pre hodnotenú pomôcku
- Údajmi uvedenými v súbore(-och) o riadení rizík
- Údajmi uvedenými na označení a/alebo v návode na použitie (t. j. reziduálne riziká, ktoré sa majú oznámiť používateľovi sú adresované).

Klinická bezpečnosť sa preukázala nízkymi mierami komplikácií identifikovanými v publikovanej recenzovanej klinickej literatúre, v klinických štúdiách zadávaných spoločnosťou, v prieskumoch údajov po uvedení na trh spolu so žiadnym stiahnutím z trhu. Neboli zistené žiadne výhrady týkajúce sa výkonnosti, preskúmaná literatúra obsahovala použitie pomôcky FemoSeal™ VCS, ktoré bolo v súlade s určeným použitím výrobcu.

## **1.5 Možné diagnostické alebo terapeutické alternatívy**

Po cievnej katetrizácii sa na dosiahnutie hemostázy v mieste arteriotómie tradične používa manuálna kompresia. Manuálna kompresia je spojená s dlhodobou imobilizáciou pacienta (až 8 hodín po zákroku) a so značným nepohodlím a dlhšou hospitalizáciou. v nedávnom systematickom prieskume sa zistilo, že medián času na dosiahnutie hemostázy s manuálnou kompresiou bol 20,8 minúty.<sup>1</sup>

Medzi alternatívy k manuálnej kompresii patria externé pomôcky na dosiahnutie hemostázy, ktoré aplikujú mechanickú kompresiu na miesto arteriotómie. Tieto pomôcky neskracujú čas na dosiahnutie hemostázy ani čas na dosiahnutie ambulácie, znižujú však nároky na personál nahradením manuálnej kompresie mechanickou kompresiou. Miery výskytu nežiaducich udalostí

súvisiacich s použitím mechanickej kompresie sú podobná mieram výskytu súvisiacim s použitím manuálnej kompresie.

Cievne uzatváracie pomôcky, ako je FemoSeal™ VCS, sú určené na uzavretie arteriotómie. Cieľom je skrátiť čas potrebný na dosiahnutie hemostázy a umožniť skoršiu ambuláciu. Nedávna systematická recenzia zahŕňajúca 13 komerčne dostupných pomôcok zistila, že medián času na dosiahnutie hemostázy s pomôckou na uzavretie ciev bol 5,4 minúty. Medián času na dosiahnutie hemostázy pre jednotlivé pomôcky na uzavretie ciev sa pohyboval od 1 minúty (FemoSeal™ VCS) do 14 minút; pričom pre väčšinu pomôcok je od 4 do 10 minút.<sup>1</sup>

Najčastejšie hlásené nežiaduce udalosti spojené so uzavretím miesta arteriotómie s manuálnymi kompresiami, externými hemostatickými pomôckami alebo pomôckami na uzavretie ciev zahŕňajú hematóm, krvácanie v mieste prístupu, pseudoaneuryzmu, arteriovenóznú fistulu a infekciu. Rovnaký systematický prehľad (34 randomizovaných kontrolovaných štúdií, 14 401 pacientov) zistil, že miery nežiaducich udalostí boli podobné medzi manuálnou kompresiou a použitím pomôcok na uzavretie ciev, s výnimkou toho, že krvácanie malo tendenciu byť o niečo vyššie pri pomôckach na uzavretie ciev.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Odporúčaný profil používateľa a školenie

Určenými používateľmi cievneho uzatváracieho systému FemoSeal™ Vascular Closure System sú lekári vyškolení na vykonávanie arteriálneho prístupu a uzatváranie endovaskulárnych zákrokov prostredníctvom spoločnej femorálnej artérie a zúčastnili sa školenia lekárov o používaní pomôcky FemoSeal™ od spoločnosti Terumo Medical Corporation.

## 1.7 Relevantné harmonizované a bežné normy

| Označenie normy | Aktuálny rok súladu/revízia | Popis                                                                                                |
|-----------------|-----------------------------|------------------------------------------------------------------------------------------------------|
| ISO 11070       | 2014/AMD1:2018              | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                  |
| EN ISO 11070    | 2014/A1:2018                | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                  |
| Usmernenie FDA  | 20. máj 2021                | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment |

| Označenie normy | Aktuálny rok súladu/revízia | Popis                                                                                                                                                                    |
|-----------------|-----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F2052      | 2015                        | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment                                 |
| ASTM F2213      | 2017                        | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment                                             |
| ASTM F2503      | 2020                        | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                                                           |
| ASTM F2182      | 2019                        | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging                                    |
| EN ISO 13485    | 2016/A11:2021               | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 13485       | 2016                        | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 14644-1     | 2015                        | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1  | 2015                        | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2     | 2015                        | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2  | 2015                        | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3     | 2019                        | Cleanrooms and associated controlled environments — Part 3: Testovacie metódy                                                                                            |

| Označenie normy        | Aktuálny rok súladu/revízia | Popis                                                                                                                                         |
|------------------------|-----------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 14644-3         | 2019                        | Cleanrooms and associated controlled environments — Part 3: Testovacie metódy                                                                 |
| ISO 14698-1            | 2003                        | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                         |
| EN ISO 14698-1         | 2003                        | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                         |
| ISO 14698-2            | 2003/TC1:2004               | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| EN ISO 14698-2         | 2003/TC 1:2004              | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| USP <788>              | N/A                         | PARTICULATE MATTER IN INJECTIONS                                                                                                              |
| EU Pharmacopeia 2.9.19 | N/A                         | Particulate Contamination: Sub-Visible Particles                                                                                              |
| IEC 62366-1            | 2015                        | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN 62366-1             | 2015                        | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN ISO 14971           | 2019/A11:2021               | Medical devices — Application of risk management to Medical devices                                                                           |
| ISO 14971              | 2019                        | Medical devices — Application of risk management to Medical devices                                                                           |
| ASTM F1980             | 2016                        | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                                           |
| EN ISO 10993-1         | 2020                        | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process                                    |



| Označenie normy | Aktuálny rok súladu/revízia | Popis                                                                                                                |
|-----------------|-----------------------------|----------------------------------------------------------------------------------------------------------------------|
| ISO 10993-1     | 2018                        | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2  | 2006                        | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2     | 2006                        | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3  | 2014                        | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3     | 2014                        | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4  | 2017                        | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4     | 2017                        | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| EN ISO 10993-5  | 2009                        | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| ISO 10993-5     | 2009                        | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| EN ISO 10993-6  | 2016                        | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |
| ISO 10993-6     | 2016                        | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |
| EN ISO 10993-10 | 2023                        | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                       |
| ISO 10993-10    | 2021                        | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                       |
| EN ISO 10993-11 | 2018                        | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                      |



| Označenie normy | Aktuálny rok súladu/revízia | Popis                                                                                                                                      |
|-----------------|-----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-11    | 2017                        | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| EN ISO 10993-12 | 2021                        | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| ISO 10993-12    | 2021                        | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| EN ISO 10993-17 | 2009                        | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17    | 2002                        | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18    | 2020/A1:2022                | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |
| EN ISO 10993-18 | 2020/A1:2022                | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |
| EN ISO 10993-23 | 2021                        | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |
| ISO 10993-23    | 2021                        | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |
| ASTM F2382      | 2018                        | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)          |
| ASTM F756       | 2017                        | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                      |
| USP <85>        | N/A                         | [Bacterial Endotoxins Test. (Sterility)]                                                                                                   |

| Označenie normy | Aktuálny rok súladu/revízia | Popis                                                                                                                                                                        |
|-----------------|-----------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| USP <161>       | N/A                         | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72  | 2019                        | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135    | 2014/A1:2019                | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135       | 2014/A1:2018                | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7  | 2008/A1:2022                | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |
| ISO 10993-7     | 2008/A1:2019                | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                                            |
| EN 556-1        | 2024                        | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices              |
| EN ISO 11737-1  | 2018/A1:2021                | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                                        |
| ISO 11737-1     | 2018/A1:2021                | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                                        |
| EN ISO 11138-1  | 2017                        | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                                 |
| ISO 11138-1     | 2017                        | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                                 |

| Označenie normy   | Aktuálny rok súladu/revízia | Popis                                                                                                                                    |
|-------------------|-----------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 11138-2    | 2017                        | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| ISO 11138-2       | 2017                        | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| EN ISO 15223-1    | 2016                        | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| ISO 15223-1       | 2016                        | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| EN 1041           | 2008/A1:2013                | Information supplied by the manufacturer of medical devices                                                                              |
| EN ISO 11607-1    | 2020/A1:2023                | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| ISO 11607-1       | 2019/A1:2023                | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| EN ISO 11607-2    | 2020/A1:2023                | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes       |
| ISO 11607-2       | 2019/A1:2023                | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes       |
| ASTM D4169        | 2016                        | Standard Practice for Performance Testing of Shipping Containers and Systems                                                             |
| ASTM F1886/F1886M | 2016                        | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                      |

| Označenie normy | Aktuálny rok súladu/revízia | Popis                                                                                                                                                                              |
|-----------------|-----------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F2825      | 2018                        | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                           |
| ASTM F2096      | 2011 (R 2019)               | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                                       |
| ASTM F88/F88M   | 2015                        | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                               |
| MDCG 2021-24    | 2021                        | Guidance on classification of medical devices                                                                                                                                      |
| MDCG 2020-3     | 2020                        | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD         |
| MDCG 2020-8     | 2020                        | Post-market clinical follow-up (PMCF) Evaluation Report Template a guide for manufacturers and notified bodies                                                                     |
| MDCG 2020-7     | 2020                        | Post-market clinical follow-up (PMCF) Plan Template a guide for manufacturers and notified bodies                                                                                  |
| MDCG 2020-6     | 2020                        | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                               |
| MDCG 2019-9 v1  | 2022                        | Summary of safety and clinical performance a guide for manufacturers and notified bodies                                                                                           |
| MDCG 2019-8 v2  | 2020                        | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices |
| MDCG 2020-15    | 2020                        | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                           |
| MDCG 2021-11    | 2021                        | Guidance on Implant Card – ‘Device types’                                                                                                                                          |

| Označenie normy      | Aktuálny rok súladu/revízia | Popis                                                                                                                                                                                                                                                         |
|----------------------|-----------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2021-19         | 2021                        | Guidance note integration of the UDI within an organisation's quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4       | 2021                        | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2          | 2019                        | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1          | 2019                        | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7          | 2018                        | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part a Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6          | 2018                        | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |
| MDCG 2018-4          | 2018                        | MDCG 2018-4 Annex: UDI database Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                                                                                                  |
| MDCG 2018-3 v1       | 2020                        | Guidance on UDI for systems and procedure packs                                                                                                                                                                                                               |
| MDCG 2021-25         | 2021                        | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC                                                                 |
| Meddev 2.12-2 Rev. 2 | 2012                        | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                                                                                        |

## 2.0 LITERATÚRA

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### 3.0 HISTÓRIA ZMIEN

| Číslo revízie SSCP       | Dátum vydania   | Popis zmeny                                                         | Revízia schválená notifikovaným orgánom                                                                                                                                                                                                                                                                                                               |
|--------------------------|-----------------|---------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022             | 20. január 2023 | Prvé vydanie na základe osvedčenia MDR CE                           | <p><input checked="" type="checkbox"/> Áno</p> <p>Jazyk validácie: English</p> <p><input type="checkbox"/> Nie [platí len pre pomôcky triedy IIa alebo niektoré implantovateľné pomôcky triedy IIb (MDR, článok 52 (4) 2. odsek), pre ktoré ešte nie je SSCP schválený notifikovaným orgánom]</p> <p><input type="checkbox"/> Iné (špecifikujte):</p> |
| SSCP-FS-2023 – Revízia 1 | 15. marec 2024  | Aktualizované pre obdobie od 1. januára 2019 do 31. decembra 2023.  | <p><input checked="" type="checkbox"/> Áno</p> <p>Jazyk validácie: English</p> <p><input type="checkbox"/> Nie [platí len pre pomôcky triedy IIa alebo niektoré implantovateľné pomôcky triedy IIb (MDR, článok 52 (4) 2. odsek), pre ktoré ešte nie je SSCP schválený notifikovaným orgánom]</p> <p><input type="checkbox"/> Iné (špecifikujte):</p> |
| SSCP-FS-2024 Revízia 1   |                 | Aktualizované pre obdobie od 1. septembra 2019 do 31. augusta 2024. | <p><input type="checkbox"/> Áno</p> <p>Jazyk validácie: English</p> <p><input type="checkbox"/> Nie [platí len pre pomôcky triedy IIa alebo niektoré implantovateľné pomôcky triedy IIb (MDR, článok 52 (4) 2. odsek), pre ktoré ešte nie je SSCP schválený notifikovaným orgánom]</p> <p><input type="checkbox"/> Iné (špecifikujte):</p>            |

|                           |               |                                                |                                                                                                                                                                                                                                                                                                                                            |
|---------------------------|---------------|------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>Revízia 2 | June 20, 2025 | Revidované na základe otázok NSAI na validáciu | <input checked="" type="checkbox"/> Áno<br>Jazyk validácie: English<br><br><input type="checkbox"/> Nie [platí len pre pomôcky triedy IIa alebo niektoré implantovateľné pomôcky triedy IIb (MDR, článok 52 (4) 2. odsek), pre ktoré ešte nie je SSCP schválený notifikovaným orgánom]<br><br><input type="checkbox"/> Iné (špecifikujte): |
|---------------------------|---------------|------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

**Povzetek o varnosti in klinični učinkovitosti**  
**Sistem žilnega zapirala FemoSeal™ Vascular Closure System**

|                                                       |                                                                                              |
|-------------------------------------------------------|----------------------------------------------------------------------------------------------|
| <b>Proizvajalec</b>                                   | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873, ZDA         |
| <b>SRN proizvajalca</b>                               | US-MF-000019594                                                                              |
| <b>Predstavnik vodstva/PRRC</b>                       | Kimberly Feitl<br>Vice President, Quality                                                    |
| <b>Osnovni UDI-DI</b>                                 | 38970FS79                                                                                    |
| <b>Številka EMDN</b>                                  | C900199 – Haemostasis systems - other                                                        |
| <b>Razred pripomočka</b>                              | Razred III                                                                                   |
| <b>Leto prve označitve pripomočka<br/>z oznako CE</b> | 2005                                                                                         |
| <b>Predstavnik v EU</b>                               | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgija<br>SRN: BE-AR-000001433 |
| <b>Priglašeni organ</b>                               | NSAI<br>CE 0050                                                                              |

## Kazalo vsebine

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Ta povzetek o varnosti in klinični učinkovitosti (SSCP – Summary of Safety and Clinical Performance) zagotavlja javni dostop do posodobljenega povzetka glavnih vidikov varnosti in klinične učinkovitosti sistema žilnega zapirala FemoSeal™ Vascular Closure System (VCS).

Povzetek o varnosti in klinični učinkovitosti pripomočka, ki je namenjen uporabnikom/zdravstvenim delavcem, je na voljo spodaj v **razdelku 1.0**.

## **1.0 POVZETEK ZA UPORABNIKE/ZDRAVSTVENE DELAVCE**

SSCP ne nadomešča navodil za uporabo kot glavnega dokumenta za zagotovitev varne uporabe pripomočka, niti ni namenjen zagotavljanju diagnostičnih ali terapevtskih predlogov za predvidene uporabnike ali paciente. SSCP ne nadomešča obveznih podatkov na karticah vsadkov ali v drugih obveznih dokumentih.

### **1.1 Predvidena uporaba pripomočka**

#### **1.1.1 Predvidena uporaba**

Sistem žilnega zapirala FemoSeal™ Vascular Closure System je medicinski pripomoček, namenjen zaprtju arterijske punkcije po perkutani kateterizaciji skozi skupno femoralno arterijo.

#### **1.1.2 Indikacije za uporabo**

Sistem žilnega zapirala FemoSeal™ Vascular Closure System je indiciran za uporabo pri zapiranju skupne femoralne arterijske punkcije (arteriotomije) pri pacientih, pri katerih je bila opravljena perkutana kateterizacija z uporabo žilnega uvajala 7 Fr (2,33 mm) ali manjšega.

#### **1.1.3 Kontraindikacije in/ali omejitve**

Sistem žilnega zapirala FemoSeal™ Vascular Closure System je kontraindiciran pri pacientih z arteriotomijami, pri katerih so bila uporabljena uvajala ali pripomočki, večji od 7 Fr (2,33 mm).

#### **1.1.4 Ciljne populacije pacientov**

Varnost in učinkovitost sistema žilnega zapirala FemoSeal™ Vascular Closure System je bila ugotovljena pri pacientih, starih 18 let in več, pri katerih je bila opravljena perkutana kateterizacija z uporabo žilnega uvajala 7 Fr (2,33 mm) ali manjšega.

#### **1.1.5 Posebne populacije pacientov**

Varnost in učinkovitost sistema žilnega zapirala FemoSeal™ Vascular Closure System ni bila ugotovljena pri naslednjih populacijah pacientov:

- pacientih z že obstoječo avtoimunsko boleznijo;
- pacientih, pri katerih je bila izvedena terapevtska tromboliza;
- pacientih s klinično pomembno periferno arterijsko boleznijo;
- pacientih z nenadzorovano hipertenzijo (sistolično > 220 mmHg ali diastolično > 110 mmHg);
- pacientih z motnjo krvavitve, vključno s trombocitopenijo (< 100.000 trombocitov) ali anemijo (Hgb < 10 mg/dl);

- pacientih z notranjo svetlino skupne femoralne arterije, manjšo od 5 mm;
- pacientih z okvaro ledvic in/ali jeter;
- pacientih z drugimi pomembnimi sočasnimi boleznimi;
- populaciji z določenim rasnim in/ali etničnim poreklom;
- pacientih, ki so v zadnjih 72 urah doživeli miokardni infarkt;
- pacientih z žilnim presadkom ali stentom na mestu punkcije;
- pacientkah, ki so noseče ali dojijo;
- pacientih, mlajših od 18 let.

### 1.1.6 Predvideni uporabniki

Predvideni uporabniki sistema žilnega zapirala FemoSeal™ Vascular Closure System so zdravniki, ki so usposobljeni za izvajanje arterijskega pristopa in zapiranja pri endovaskularnih posegih skozi skupno femoralno arterijo in so se udeležili programa usposabljanja zdravnikov za uporabo pripomočkov FemoSeal™ družbe Terumo Medical Corporation.

## 1.2 Opis pripomočka

### 1.2.1 Opis pripomočka

Sistem žilnega zapirala FemoSeal™ Vascular Closure System, ki ga proizvaja Terumo Medical Corporation (TMC), je resorbilno žilno zapiralo, zasnovano za doseganje femoralne arterijske hemostaze po perkutani kateterizaciji skozi skupno femoralno arterijo.

Zapiralni elementi FemoSeal™ so sestavljeni iz dveh resorbilnih polimernih ploščic, notranjega tesnila in zunanje zaklepne ploščice, ki ju skupaj drži resorbilni multifilament, s čimer se arteriotomija mehansko zapre (glejte **sliko 1.1** in **sliko 1.2**). Zunanja zaklepna ploščica se po namestitvi skozi uvajalo stožčastega ohišja pritisne na multifilamentno os, zaradi česar se mesto punkcije med notranjo in zunanjo zaklepno ploščico mehansko zapre. Zaradi trenja na multifilamentni osi notranje tesnilo in zunanja zaklepna ploščica ostaneta na svojem mestu. Hemostaza se doseže z mehanskimi sredstvi. Zapiralni elementi se razgradijo s hidrolizo.

Vsadni zapiralni komponenti, notranje tesnilo in zunanja zaklepna ploščica, se razgradita v osemnajstih (18) mesecih, medtem ko se multifilament po ocenah razgradi in absorbira s hidrolizo okoliškega tkiva po dveh (2) do treh (3) letih. Sposobnost vsadnih zapiralnih komponent, da ohranjajo kompresijo na mestu arteriotomije, je bila preizkušena do osem (8) ur. Razgradni produkti se presnovijo in izločijo z urinom ali izdihajo kot ogljikov dioksid skozi pljuča. v študijah na živalih niso opazili učinkov kopičenja. Dodatne komponente FemoSeal™, ki bodo

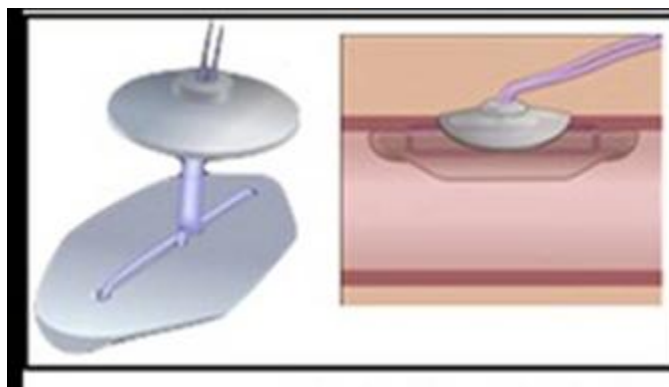


med posegom prišle v stik z živim tkivom ali krvjo, so uvajalo stožčastega ohišja, dilatator, cevka za stisnjenje, potiskalo in vodilna žica.

**Slika 1.1 Notranje tesnilo in zunanja zaklepna ploščica**

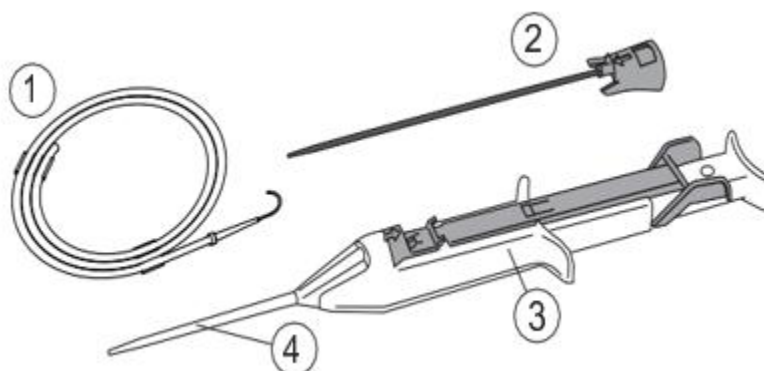


**Slika 1.2 Namestitev notranjega tesnila in zunanje zaklepne ploščice**



Enota FemoSeal™ je pakirana skupaj z dilatatorjem, vodilno žico z zunanjim premerom 0,038" (0,97 mm) in dolžine 27,5" (70 cm) ter J-ravnalom; glejte **slika 1.3** spodaj. Vodilna žica je v polietilenski cevki. Vsi deli so pakirani na pritrjenem papirnatem pladnju. Pakiranje vsebuje tudi kartico o vsadku za pacienta. Sistem žilnega zapirala FemoSeal™ Vascular Closure System ne zahteva dodatnega pribora, da bi pripomoček deloval, kot je predvideno, pripomoček pa je namenjen le uporabi z dilatatorjem in vodilno žico, ki sta priložena v pakiranju izdelka.

**Slika 1.3 Enota FemoSeal™ VCS z vodilno žico in dilatatorjem**



### 1.2.2 Surovine in komponente

V spodnji preglednici 1.1 so navedene komponente sistema FemoSeal™ VCS.

**Preglednica 1.1 Surovine in komponenta sistema FemoSeal™ VCS**

| Številka dela | Opis                                                  |                                                                 | Materiali                                                                                                                                                                 |
|---------------|-------------------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1             | Vodilna žica s premerom 0,038" (0,97 mm) z J-ravnalom |                                                                 | Vodilna žica: nerjavno jeklo 304<br>J-ravnalo: polipropilen, vijolični pigment<br>Sponka: polietilen<br>Cevke: polietilen                                                 |
| 2             | Dilatator FemoSeal                                    |                                                                 | Obod: tetrahidrofur, modri pigment, polibutilen tereftalat (PBT)<br><br>Cevka: polietilen velike gostote (HDPE), črni pigment<br><br>Mazivo: silikon, Dow Corning 360     |
| 3/4           | Enota FemoSeal                                        | Oblikovani RD7 – notranje tesnilo in zunanja zaklepna ploščica* | Kopolimer glikolida, trimetilenkarbonata, ε-kaprolaktona in TMP: trimetilolpropana (iniciator)                                                                            |
|               |                                                       | Multifilament *                                                 | Segmentirani kopolimer L,L-laktida, trimetilenkarbonata, ε-kaprolaktona in 1,3-propandiola (iniciator)<br><br>Prevleka je kopolimer glikolida, ε-kaprolaktona in L-lizina |

|  |  |                            |                                                  |
|--|--|----------------------------|--------------------------------------------------|
|  |  | Cevka za stisnjenje        | Polipropilen                                     |
|  |  | Potiskalo                  | Nerjavno jeklo 304V                              |
|  |  | Drsnik                     | Polibutilen tereftalat (PBT)                     |
|  |  | Ohišje                     | Polibutilen tereftalat (PBT)                     |
|  |  | Gumb                       | Polibutilen tereftalat (PBT)                     |
|  |  | Pokrovček gumba            | Polioksimetilen (POM)/poliacetalni kopolimer     |
|  |  | Tulec                      | Polibutilen tereftalat (PBT)                     |
|  |  | Distančnik                 | Polibutilen tereftalat (PBT)                     |
|  |  | Stožec                     | Polipropilen                                     |
|  |  | Pokrov ohišja              | Polibutilen tereftalat (PBT)                     |
|  |  | Varovalo                   | Polibutilen tereftalat (PBT), modri pigment      |
|  |  | Pokrov tulca               | Polibutilen tereftalat (PBT)                     |
|  |  | Tesnilo cevke              | Silikon, trdota po Shoru A 70                    |
|  |  | Tesnilo ohišja             | Silikon, trdota po Shoru A 50                    |
|  |  | Vzmet                      | Nerjavno jeklo 302                               |
|  |  | Uvajalo stožčastega ohišja | Polipropilen<br>Silikon, Dow Corning 360, heksan |

\* Vsadni del pripomočka; vsadne komponente so varne za slikanje z MR

Sistem FemoSeal™ VCS je steriliziran z etilenoksidom (EO) in je medicinski pripomoček za enkratno uporabo. Sistem FemoSeal™ VCS je zasnovan tako, da ga ni mogoče ponovno uporabiti.

### **Način delovanja**

FemoSeal™ VCS spodbuja mehansko hemostazo z nameščenimi zapiralnimi elementi znotraj in zunaj skupne femoralne arterije. Notranje tesnilo, ki zapre mesto punkcije, in zunanja zaklepna ploščica, ki drži notranje tesnilo na mestu, zagotavljata mehanizem za preprečevanje krvavitve.

### **1.2.3 Klinična korist**

FemoSeal™ VCS zagotavlja naslednje klinične koristi v primerjavi z zaprtjem žil po punkciji skupne femoralne arterije:

- Krajši čas do hemostaze<sup>1</sup>
- Krajši čas do hoje<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

#### 1.2.4 Predhodna(-e) generacija(-e) ali različice

- Prva različica sistema FemoSeal™ VCS (št. 11200) je bila na evropskem trgu naprodaj v letu 2005 in nekaj časa v letu 2006.
- Trenutni sistem FemoSeal™ VCS (št. 11202), ki ima izboljšan uvajalni sistem, je na trgu od 28. marca 2006.

#### 1.2.5 Dodatki, namenjeni uporabi v kombinaciji s pripomočkom

Enota FemoSeal™ je pakirana skupaj z dilatatorjem, vodilno žico z zunanjim premerom 0,038" (0,97 mm) in dolžine 27,5" (70 cm) ter J-ravnalom. Vodilna žica je dodatek za enoto FemoSeal™. J-ravnalo je komponenta vodilne žice, medtem ko je dilatator komponenta enote FemoSeal™. Kot dodatek se obravnava samo vodilna žica. Vodilna žica je v polietilenski cevki. Vsi deli so pakirani na pritrjenem papirnatem pladnju. Pakiranje vsebuje tudi kartico o vsadku za pacienta. Sistem žilnega zapirala FemoSeal™ Vascular Closure System ne zahteva dodatnega pribora, da bi pripomoček deloval, kot je predvideno, pripomoček pa je namenjen le uporabi z dilatatorjem in vodilno žico, ki sta priložena v pakiranju izdelka.

#### 1.2.6 Drugi pripomočki in izdelki, namenjeni uporabi v kombinaciji s pripomočkom

FemoSeal™ VCS ne potrebuje dodatnih pripomočkov za predvideno delovanje.

### 1.3 Tveganja in opozorila

#### 1.3.1 Preostala tveganja in neželeni učinki

Znani ali predvidljivi neželeni dogodki, škodljive posledice in zapleti, povezani z uporabo sistema FemoSeal™ VCS, ki so posledica preostalih tveganj, so navedeni v **preglednici 1.2**. Stopnja pojavljanja temelji na analizi dokumentacije o tveganju in se izračuna na podlagi podatkov o nadzoru po dajanju na trg od 1. septembra 2019 do 31. avgusta 2024. Za sistem FemoSeal™ VCS ni neznanih preostalih tveganj, vsa ustrezna tveganja pa so bila primerno obravnavana v navodilih za uporabo in procesu obvladovanja tveganja.

### Preglednica 1.2. Neželeni dogodki/zapleti pri pripomočku FemoSeal

| Škodljiva posledica                     | Stopnja pojavljanja (%) | Dejavniki za zmanjšanja tveganja                                                                                                                                                  |
|-----------------------------------------|-------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Alergijska reakcija                     | 0,0000                  | Ukrepi in načrti za čim večje zmanjšanje tveganja so bili obravnavani glede na značilnosti zasnove izdelka, proizvodne smernice, označevanje izdelka in usposabljanje zdravnikov. |
| Anevrizma                               | 0,0000                  |                                                                                                                                                                                   |
| AV fistula                              | 0,0001                  |                                                                                                                                                                                   |
| Izguba krvi/krvavitev                   | 0,0280                  |                                                                                                                                                                                   |
| Smrt                                    | 0,0002                  |                                                                                                                                                                                   |
| Ekhimoza                                | 0,0000                  |                                                                                                                                                                                   |
| Embolija                                | 0,0000                  |                                                                                                                                                                                   |
| Reakcija na tujke                       | 0,0000                  |                                                                                                                                                                                   |
| Hematom                                 | 0,0027                  |                                                                                                                                                                                   |
| Krvavitev                               | 0,0001                  |                                                                                                                                                                                   |
| Okužba                                  | 0,0002                  |                                                                                                                                                                                   |
| Vnetna reakcija                         | 0,0000                  |                                                                                                                                                                                   |
| Odrevenelost                            | 0,0000                  |                                                                                                                                                                                   |
| Bolečina                                | 0,0000                  |                                                                                                                                                                                   |
| Nelagodje pacienta                      | 0,0004                  |                                                                                                                                                                                   |
| Odložitev posega                        | 0,0065                  |                                                                                                                                                                                   |
| Psevdoanevrizma                         | 0,0004                  |                                                                                                                                                                                   |
| Retroperitonealna krvavitev             | 0,0002                  |                                                                                                                                                                                   |
| Sepsa                                   | 0,0000                  |                                                                                                                                                                                   |
| Tromboembolija                          | 0,0000                  |                                                                                                                                                                                   |
| Tromboza                                | 0,0001                  |                                                                                                                                                                                   |
| Okluzija žile/ishemija spodnjih okončin | 0,0002                  |                                                                                                                                                                                   |
| Perforacija žile                        | 0,0000                  |                                                                                                                                                                                   |
| Disekcija/laceracija žilnega tkiva      | 0,0003                  |                                                                                                                                                                                   |

### 1.3.2 Opozorila in previdnostni ukrepi

#### Opozorila

1. Ne uporabljajte, če je embalaža poškodovana ali če sterilna pregrada ni nepoškodovana.
2. Ne uporabljajte po izteku roka uporabnosti – biorazgradljive komponente morda ne bodo pravilno delovale.
3. Ne uporabljajte, če je kateri koli izdelek poškodovan ali ima kakršno koli napako.
4. Uporaba sistema žilnega zapirala FemoSeal™ Vascular Closure System, pri kateri lahko pride do bakterijske kontaminacije žilnega uvajala ali okoliškega tkiva, lahko povzroči okužbo.
5. Če obstaja sum, da je bila posteriorna stena arterije prebodena, ali je bilo opravljenih več arterijskih punkcij, se za doseganje arterijske hemostaze ne zanašajte samo na sistem žilnega zapirala FemoSeal™ Vascular Closure System. Uporabite dodatno ročno ali mehansko kompresijo.
6. Če je mesto punkcije na bifurkaciji femoralne arterije ali distalno od nje, ne smete uporabiti sistema žilnega zapirala FemoSeal™ Vascular Closure System zaradi nevarnosti nepravilne namestitve notranjega tesnila. Ta dogodek lahko povzroči zaplete zaradi krvavitve in/ali motnje normalnega pretoka krvi.
7. Če se arterijska krvavitev iz mesta reza nadaljuje, multifilamenta ne prerežite, dokler ne dosežete hemostaze. Če hemostaza ni dosežena, pritrdite multifilament s sterilno oblogo za rano in izvajajte dodatno kompresijo, dokler ne dosežete hemostaze. v primeru vztrajne arterijske krvavitve lahko pride do pomembnih zapletov, ki lahko povzročijo poškodbe ali smrt pacienta.
8. Sistema žilnega zapirala FemoSeal™ Vascular Closure System ne uporabljajte, če je mesto punkcije proksimalno od ingvinalnega ligamenta, saj lahko pride do retroperitonealnega hematoma.
9. Pri pacientih z večjim tveganjem za krvavitev lahko pride do večje izgube krvi, zaradi česar je lahko potrebna transfuzija.
10. Če se notranja ploščica sname, lahko povzroči trombotični in/ali embolični dogodek.

#### Previdnostni ukrepi

1. Poseg namestitve sistema žilnega zapirala FemoSeal™ Vascular Closure System morajo izvesti zdravniki, ki so ustrezno usposobljeni za uporabo pripomočka.
2. Pred namestitvijo sistema žilnega zapirala FemoSeal™ Vascular Closure System opravite omejen femoralni angiogram ali ultrazvočno vodeno femoralno punkcijo.

3. Poseg prekinite, če:
  - je premer svetline skupne femoralne arterije  $< 5$  mm;
  - je v bližini mesta punkcije skupne femoralne arterije prisotna stenoza in/ali pomemben plak;
  - je arterijska punkcija na bifurkaciji femoralne arterije ali distalno od nje;
  - so v bližini mesta punkcije skupne femoralne arterije anomalne veje ali nepravilnosti žil.
4. Če je prisoten kakršen koli hematoma, je potrebna posebna previdnost pri pravilnem vstavljanju uvajala stožčastega ohišja v arterijo.
5. Uporabite tehniko punkcije samo ene stene. Ne prebodite posteriorne stene arterije.
6. Pri uporabi sistema žilnega zapirala FemoSeal™ Vascular Closure System vedno uporabljajte sterilno tehniko.
7. Sistem žilnega zapirala FemoSeal™ Vascular Closure System je namenjen samo za enkratno uporabo in ga ni dovoljeno ponovno sterilizirati ali na kakršen koli način ponovno uporabiti. Enota FemoSeal™ je zasnovana tako, da je ni mogoče ponovno uporabiti.
8. Če pri nameščanju notranjega tesnila naletite na nepričakovan upor, prekinite poseg.
9. Za pravilno namestitev notranjega tesnila prestavite svoj palec tako, da lahko gumb prosto odskoči.
10. Pred namestitvijo zunanje zaklepne ploščice se prepričajte, da je uvajalo stožčastega ohišja enote FemoSeal™ pod površino kože. Pri pacientih s kratko razdaljo med femoralno arterijo in kožo se lahko zunanja zaklepna ploščica nenamerno namesti nad raven kože.
11. Za pravilno namestitev bo morda pred namestitvijo potreben kožni rez.
12. Če je notranje tesnilo znotraj arterije, vendar ni mogoče popolnoma pritisniti gumba in namestiti zunanje zaklepne ploščice, bo za odstranitev zapiralnih elementov FemoSeal™ morda potreben kirurški poseg.
13. Če je v 18 mesecih potrebna ponovna punkcija iste femoralne arterije, jo je treba opraviti vsaj en centimeter proksimalno od prejšnjega mesta pristopa s sistemom žilnega zapirala FemoSeal™ Vascular Closure System.
14. Pacientu naročite, naj upošteva zdravnikova navodila glede pregledovanja mesta zaprtja.
15. Pacientu naročite, naj ima naslednjih 18 mesecev pri sebi kartico z informacijami za pacienta.

### **Previdnostni ukrepi ob odpustu iz bolnišnice**

Preden razmislite o odpustu iz bolnišnice, ocenite pacienta glede naslednjih kliničnih stanj:

1. krvavitve in/ali hematoma na mestu zaprtja;
2. bolečine med hojo;
3. znakov okužbe na mestu zaprtja.

### **1.3.3 Varnostni korektivni ukrepi**

V obdobju od 1. septembra 2019 do vključno 31. avgusta 2024 je bil izveden en varnostni korektivni ukrep v zvezi s sistemom FemoSeal™ VCS.

Leta 2022 je družba Terumo prostovoljno odpoklicala sistem FemoSeal™ VCS zaradi pritožb glede napak pri testiranju postopka in testiranju ob sprostitvi serij izdelka FemoSeal proizvajalca Elkton, predvidenega za merjenje sile stiskanja in uvlečne sile. s trga Južne Koreje je bilo odpoklicanih skupno 950 enot.

## **1.4 Klinično vrednotenje in klinično spremljanje po dajanju na trg**

**Preglednica 1.3** vsebuje seznam ključnih študij, ki so bile izvedene za pridobitev dovoljenja za dajanje sistema FemoSeal™ VCS na trg, ter študij po dajanju pripomočka na trg in dejavnosti kliničnega spremljanja po dajanju na trg. Različica pripomočka, uporabljena v študiji, je navedena v spodnji preglednici. Prva različica sistema FemoSeal™ VCS (št. 11200) je bila na trgu do leta 2006, medtem ko je bila naslednja različica (št. C11202) dana na trg leta 2006 in je trenutno na trgu.

### **Preglednica 1.3 Povzetek ključnih študij**

| <b>Funkcionalno testiranje na živalih pred dajanjem na trg</b>                                                                                                                                                                                                          | <b>Različica pripomočka</b> |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                       |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                       |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                       |
| <b>Prva klinična študija pri ljudeh</b>                                                                                                                                                                                                                                 |                             |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                       |



| Zaključene klinične študije po dajanju na trg                                                                                   |                                    |
|---------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                      | C11202<br>(trenutni<br>pripomoček) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                               | C11202<br>(trenutni<br>pripomoček) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | C11202<br>(trenutni<br>pripomoček) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)          | C11202<br>(trenutni<br>pripomoček) |
| Načrtovane/potekajoče klinične študije po dajanju na trg                                                                        |                                    |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                      | C11202<br>(trenutni<br>pripomoček) |
| Dejavnosti kliničnega spremljanja po dajanju na trg                                                                             |                                    |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(trenutni<br>pripomoček) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(trenutni<br>pripomoček) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(trenutni<br>pripomoček) |

#### 1.4.1 Povzetek podatkov iz študij pred dajanjem na trg (testiranje na živalih in klinične raziskave)

V preglednici 1.4 spodaj so opisane vse študije pred dajanjem na trg, tako testiranja na živalih kot klinične raziskave.

**Preglednica 1.4 Povzetki študij pred dajanjem na trg**

| Funkcionalno testiranje na živalih pred dajanjem na trg                                        |                                    |                                             |                                                                                                                        |                                                    |                                                                                                                                            |
|------------------------------------------------------------------------------------------------|------------------------------------|---------------------------------------------|------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| Ime študije                                                                                    | Leto/<br>informacije o<br>podjetju | Vrsta študije                               | Cilji                                                                                                                  | Mejniki                                            | Možna merila<br>sprejemljivosti                                                                                                            |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the | 2000<br>Radi Medical<br>System AB  | Študija na živalih;<br>raziskovalna študija | Namen študije je bil oceniti biokompatibilnost in biofunkcionalnost biorazgradljivega vsadka, zasnovanega za doseganje | N = 3 odrasle samice ovc, 1 žival na časovno točko | Prehodnost arterije<br>• Ocena pretoka krvi po namestitvi – zmanjšanje pretoka krvi pri 2/3, kar je bilo povezano z začasnimi arterijskimi |

|                                                                                                                                                                          |                                      |  |                                                                                                       |                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
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| Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | Izvedlo podjetje Biomatech, Francija |  | hemostaze v ožilju. Poročilo obravnava rezervne živali iz študije številka 862 (dokument št. 1051-01) | <p>Spremljanje za histopatološko analizo, makroskopsko oceno in ultrastrukturno analizo</p> <ul style="list-style-type: none"> <li>• 12 mesecev</li> <li>• 15 mesecev</li> <li>• 18 mesecev</li> </ul> <p>Spremljanje z barvnim Dopplerjevim ultrazvokom – 30 dni na mestih karotidnega in femoralnega arterijskega pristopa</p> | <p>vazospazmom, ki so ga pripisali posegu; do obeh je prišlo na levi skupni karotidni arteriji</p> <ul style="list-style-type: none"> <li>• Ocena z barvnim Dopplerjevim ultrazvokom (4 tedne) – pri 3/3 (100 %) brez večjega zmanjšanja pretoka krvi 30 dni po vsaditvi</li> </ul> <p>Makroskopske ugotovitve</p> <ul style="list-style-type: none"> <li>• 12 mesecev – prehodnost je bila makroskopsko potrjena z odsotnostjo anatomsko vidne okluzije; brez makroskopskih sprememb zaradi lokalnega neprenašanja (krvavitev, nekroza ali neovaskularizacija); enkapsulacija notranje ploščice je bila izrazita</li> <li>• 15 mesecev – makroskopsko opazovanje ni pokazalo znakov vnetja; brez ugotovljenih ostankov notranjih ali zunanjih ploščic; enkapsulacija tkiva na predelu zunanje ploščice je bila videti enako kot pri 12-mesečnem opazovanju</li> <li>• 18 mesecev – makroskopsko opazovanje ni pokazalo znakov lokalnega neprenašanja, zunanja ploščica je bil vidna (3/3 primerov), popolna razgradnja notranje ploščice; 1/3 (leva skupna karotidna arterija) – na mestu vsadka je bilo opaziti depresijo stene arterije (lahko je bila povezana z namestitvijo pripomočka)</li> </ul> <p>Zaključki</p> <ul style="list-style-type: none"> <li>• Makroskopsko 12, 15 in 18 mesecev po vsaditvi niso odkrili nobenih nekrotičnih, degenerativnih ali trombotičnih znakov.</li> <li>• Proces razgradnje notranje in zunanje ploščice je napredoval</li> </ul> |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|--|-------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

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|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|-------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                                                                                                |                                                                                |                                                 |                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                           | <p>med 12. in 18. mesecem in je bil po 18 mesecih končan, pri čemer je območje vsaditve prekrivalo belkasto tkivo.</p> <ul style="list-style-type: none"> <li>Histološko po 18 mesecih polimerni material ni bil več viden, prisotno pa je bilo endoluminalno fibrozno tkivo. Nekrotičnih, degenerativnih ali trombotičnih sprememb ni bilo zaznati.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002 Radi Medical System AB</p> <p>Izvedlo podjetje Biomatech, Francija</p> | <p>Študija na živalih; raziskovalna študija</p> | <p>Namen študije je bil oceniti biokompatibilnost biorazgradljivega vsadka, zasnovanega za doseganje hemostaze v ožilju.</p> | <p>Spremljanje (po vsaditvi)</p> <ul style="list-style-type: none"> <li>12 tednov</li> <li>24 tednov</li> <li>36 tednov</li> </ul> <p>N = 12 ovc, 3 živali na časovno točko, 3 rezervne živali, usmrčene v 12., 15. in 18. mesecu</p> <p>Mesta vsaditve – desna in leva femoralna arterija, desna in leva skupna karotidna arterija</p> <p>Analiza z barvnim Dopplerjevim ultrazvokom</p> | <p><u>Prehodnost karotidnih in femoralnih arterij po 4 tednih</u></p> <ul style="list-style-type: none"> <li>Večje zmanjšanje pretoka krvi pri 0/12 (0 %)</li> </ul> <p><u>Brez večjega zmanjšanja pretoka krvi</u></p> <ul style="list-style-type: none"> <li>Huda motnja pretoka krvi, povezana z vstavitvijo pripomočka pri 0/12 (0 %)</li> <li>Zmanjšanje pretoka krvi v levi skupni karotidni arteriji pri 2/12 (16,6 %) zaradi začasnega arterijskega vazospazma (posledica operacije in ne pripomočka)</li> </ul> <p><u>Poslabšanje krvnega pretoka pri spremljanju</u></p> <p>12 tednov – 0/12 (0 %)</p> <p>24 tednov – 0/12 (0 %)</p> <p>36 tednov – 0/12 (0 %)</p> <p>Meritve krvnega tlaka (3 ovce – 36 tednov)</p> <ul style="list-style-type: none"> <li>Brez večjega zmanjšanja pretoka krvi</li> </ul> <p>Makroskopski podatki o integraciji in razgradnji (stopnja 0–4)</p> <p><u>Mesta na karotidni arteriji</u></p> <p><u>Notranja stran</u></p> <p>– enkapsulacija</p> <p>1,3 po 12 tednih</p> <p>0,8 po 24 tednih</p> |

|  |  |  |  |  | 0,7 po 36 tednih<br>– razgradnja materiala<br>2,2 po 12 tednih<br>2,3 po 24 tednih<br>0,7 po 36 tednih<br><i>Zunanja stran</i><br>– enkapsulacija<br>2,0 po 12 tednih<br>1,0 po 24 tednih<br>0,8 po 36 tednih<br>– razgradnja materiala<br>2,0 po 12 tednih<br>2,7 po 24 tednih<br>3,2 po 36 tednih<br><br><u>Mesta na femoralni arteriji</u><br><i>Zunanja stran</i><br>– enkapsulacija<br>1,0 po 12 tednih<br>2,7 po 24 tednih<br>1,0 po 36 tednih<br>– razgradnja materiala<br>2,0 po 12 tednih<br>2,4 po 24 tednih<br>3,0 po 36 tednih<br><br><i>Notranja stran</i><br>– enkapsulacija<br>2,0 po 12 tednih<br>1,2 po 24 tednih<br>1,0 po 36 tednih<br>– razgradnja materiala<br>1,0 po 12 tednih<br>2,2 po 24 tednih<br>3,0 po 36 tednih<br><br><u>Histološki podatki o integraciji, razgradnji in vnetnih parametrov (povprečje ustreznih vrednosti, indeks 0–4) n = 6</u><br><br><u>Mesta na karotidni arteriji</u><br><i>Zunanja fibroza</i><br>12 tednov – 2,3<br>24 tednov – 2,3<br>36 tednov – 1,8<br><i>Notranja neointima</i><br>12 tednov – 3,0<br>24 tednov – 2,7<br>36 tednov – 3,3 |
|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | Razgradnja materiala<br>12 tednov – 1,7<br>24 tednov – 3,0<br>36 tednov – 3 +<br>Vnetni parametri (makrofagi)<br>12 tednov – 3,0<br>24 tednov – 1,7<br>36 tednov – 1,7<br><u>Mesta na femoralni arteriji</u><br>Zunanja fibroza<br>12 tednov – 1,3<br>24 tednov – 1,5<br>36 tednov – 1,7<br>Notranja neointima<br>12 tednov – 3,7<br>24 tednov – 3,3<br>36 tednov – 3,8<br>Razgradnja materiala<br>12 tednov – 2,0<br>24 tednov – 3,0<br>36 tednov – 3+<br>Vnetni parametri (makrofagi)<br>12 tednov – 3,5<br>24 tednov – 1,8<br>36 tednov – 1,8<br><br><u>Histomorfološke vrednosti prehodnosti</u><br>Mesta na karotidni arteriji<br>74,0 % po 12 tednih<br>81,9 % po 24 tednih<br>89,43 % po 36 tednih<br>Mesta na femoralni arteriji<br>12 tednov – 42,2 %<br>24 tednov – 73,21 %<br>36 tednov – 78,71 %<br><br><u>Prehodnost žil z UZ (srednja vrednost v %)</u><br>Mesto na karotidni arteriji<br>94,6 % po 12 tednih<br>96,7 % po 24 tednih<br>94,7 % po 36 tednih<br>Mesta na femoralni arteriji<br>12 tednov – 66,9 %<br>24 tednov – 63,6 %<br>36 tednov – 75,1 %<br><br>Zaključki<br><ul style="list-style-type: none"> <li>Po 12., 24. ali 36. tednu niso odkrili nobenega</li> </ul> |
|--|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                                                                                                                                                                                                                                                                        |                                                                                       |                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                           | <p>pomembnega znaka lokalnega neprenašanja (odsotnost vidnih vnetnih, nekrotičnih ali degenerativnih sprememb)</p> <ul style="list-style-type: none"> <li>Pri gostitelju in pripomočku ni bilo zabeleženih nobenih pomembnih neželenih reakcij tkiva</li> <li>Razgradnja vsadka je bila po 36 tednih skoraj popolna</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|---------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002</p> <p>Radi Medical System AB</p> <p>Izvedlo podjetje Biomatech, Francija</p> | <p>Študija na živalih</p> | <p>Namen študije je bil oceniti biokompatibilnost in biofunkcionalnost biorazgradljivega vsadka, zasnovanega za doseganje hemostaze v ožilju. Preizkušeni pripomoček bi moral vstopiti v vbodno odprtino v arterijah za doseganje hemostaze. Ena ploščica je vstopila v vbodno odprtino v arteriji, druga pa je zategnila notranjo ploščico z zunanje strani arterije. Obe ploščici sta bili vstavljeni skozi uvajalni tulec. Ploščici sta bili zasnovani tako, da preprečujeta krvavitve, se zacelita v steno žile ter se na koncu razgradita in absorbirata. Študija je bila zasnovana za zbiranje in analizo podatkov po funkcionalni vsaditvi pripomočka pri ovci in prašiču za oceno sposobnosti vsadka, da ohrani fiziološko funkcijo pri uporabi v obtočilih, ugotavljanje odziva gostitelja in odziva pripomočka (fizična celovitost, tkivna enkapsulacija ob usmrtnosti) ter oceno razgradnje vsadka.</p> | <p>Obdobje vsaditve/spremljanja je bilo pri vseh živalih 5 tednov.</p> <p>4 ovce, 1 prašič</p> <p>14 zapiralnih elementov</p> <p>8 zapiralnih elementov, vsajenih v 2 ovci,</p> <p>2 zapiralna elementa, vsajena v 1 prašiča</p> <p>Kadar sta bila v isto femoralno arterijo vsajena dva zapiralna elementa, sta bila vsajena na razdalji &gt; 30 mm.</p> | <p>Zabeleženi so bili vsi neželeni znaki (vnetje, nekroza, krvavitev ali katere koli druga poškodba) in vsakršen nastanek tanke psevdointimalne plasti. Posebna pozornost je bila posvečena začetni tkivni integraciji pripomočka, s posebnim poudarkom na enkapsulaciji notranje ploščice.</p> <p>Makroskopsko niso opazili nobenih pomembnih znakov lokalnega neprenašanja ali tromboze. Makroskopsko opazovanje ni pokazalo nobene razlike med ovci in prašiči po vsaditvi zapiralnih elementov v femoralne arterije. Makroskopsko niso opazili nobenih pomembnih znakov lokalnega neprenašanja ali tromboze. Makroskopsko opazovanje ni pokazalo nobene razlike med ovci in prašiči po vsaditvi zapiralnih elementov v femoralne arterije.</p> <p>Histopatološka analiza mesta vsaditve pri ovcih ni pokazala nobenih</p> |

|                                                                                                                  |                              |                                                   |                                                                                                                              |                                                                        | <p>lokalnih neželenih reakcij. Notranja in zunanja ploščica sta pokazali znake razgradnje in sta bili v nekaterih primerih razlomljeni na manjše delce. Notranja ploščica se je popolnoma integrirala v neointimalno tkivo. Pri prašičih je histopatološka analiza pokazala nekoliko več vnetnih znakov okoli notranje in zunanje ploščice. Pri obeh vrstah živalih je bilo pri multifilamentu nekoliko več vnetnih znakov kot pri materialu ploščic, kar je pri pletenih šivih zaradi večje površine normalno.</p> <p>Prehodnost žil je bila izmerjena po 5 tednih s tremi različnimi metodami: histomorfometrično, histomorfometrično v kombinaciji z merjenjem premera žile s kaliperjem in s preiskavo z barvnim Dopplerjevim ultrazvokom. Povprečna prehodnost žil pri ovcah je bila med 60 % in 80 %, odvisno od uporabljene metode (12 opazovanj). Pri prašičih je bila povprečna prehodnost žil med 40 % in 80 % (2 opazovanji).</p> |
|------------------------------------------------------------------------------------------------------------------|------------------------------|---------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Prva klinična študija pri ljudeh</b>                                                                          |                              |                                                   |                                                                                                                              |                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Ime študije                                                                                                      | Leto/informacije o podjetju  | Vrsta študije                                     | Cilji                                                                                                                        | Mejniki                                                                | Možna merila sprejemljivosti                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After | 2004 Radi Medical Systems AB | Odperto, multicentrično preskušanje z eno skupino | Cilji študije so bili ugotoviti varnost, delovanje in učinkovitost sistema žilnega zapirala FemoSeal Vascular Closure System | 2-delna študija<br><br>Skupno n = 80<br>1. del n = 20<br>2. del n = 60 | Rezultati<br>– <u>hemostaza, dosežena s FS brez kompresije</u><br>– 1. del pri 20/20 (100 %)<br>– 2. del pri 58/60 (97 %)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |

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|---------------------------------------------------------------------------------------------|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. |  |  | (sistem FemoSeal) na splošno in še posebej zapiranih elementov pri pacientih, pri katerih so bili opravljeni diagnostični ali intervencijski kardiološki posegi na srcu z uporabo femoralnega arterijskega pristopa. | <p>Indikacije:</p> <p>1. del – diagnostična kateterizacija srca z uporabo femoralne arterije kot mesta pristopa</p> <p>2. del – pacienti, pri katerih so bili opravljeni diagnostični in intervencijski posegi na srcu, pri katerih se kot mesto pristopa uporablja femoralna arterija</p> <p>30-dnevno spremljanje</p> | <p>Srednji čas do hemostaze v času posega (2. del) – 1,0 minute (razpon takoj – 8 minut)</p> <p><u>Čas do hoje (v minutah)</u></p> <p>1. del – mediana: 33,0<br/>srednja vrednost: 67,8</p> <p>2. del – mediana: 45<br/>srednja vrednost: 87,5</p> <p><u>Pojavnost glavnih vaskularnih zapletov – 30-dnevno spremljanje</u></p> <p>1. del – brez vaskularnih zapletov pri 20/20 (100 %)</p> <p>2. del – psevdoanevrizma pri 1/59 (1,69 %)</p> <p><u>Neuspešno zdravljenje</u></p> <p>1. del – 0/20 (0 %)</p> <p>2. del – 3/60 (5 %)</p> <ul style="list-style-type: none"> <li>2 zaradi nezmožnosti doseganja hemostaze brez uporabe kompresije</li> <li>1 zaradi večjega vaskularnega zapleta, psevdoanevrizme</li> </ul> <p><u>Neprestani izcedek</u></p> <p>1. del – 0/20 (0 %)</p> <p>2. del – 8/60 (13 %)</p> <p><u>Hematom</u></p> <p>1. del – 0/20 (0 %)</p> <p>2. del – 6/60 (10 %)</p> |
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V okviru razvojnega načrta za sistem FemoSeal™ VCS pred dajanjem na trg so bili opravljeni 3 funkcionalni testi na živalih. Leta 2000 je bila pred začetkom kliničnih študij izvedena študija na živalih za oceno biološke funkcionalnosti sistema FemoSeal™ VCS. v tej študiji je bila ocenjena sposobnost zapiralnih elementov, da ohranijo fiziološko funkcijo, ter njihova razgradnja.

Po 18 mesecih material notranje in zunanje ploščice ni bil več viden, saj ga je nadomestilo endoluminalno fibrozno tkivo. Zaključimo lahko, da je bila potrjena sposobnost zapiralnega elementa sistema FemoSeal™ VCS, da ohrani fiziološko funkcijo pri uporabi v obtočilih.

Leta 2002 je bila izvedena študija na živalih za oceno biokompatibilnosti in biofunkcionalnosti biorazgradljivega vsadka FemoSeal™ VCS, zasnovanega za doseganje hemostaze v ožilju.

Če povzamemo, je bila razgradnja vsadka do 36. tedna skoraj popolna in ni bilo pomembnih neželenih reakcij tkiva.

Leta 2002 so izvedli še eno študijo na živalih za oceno biokompatibilnosti in biofunkcionalnosti biorazgradljivega vsadka FemoSeal™ VCS, zasnovanega za doseganje hemostaze v ožilju.

Po 5 tednih je bila enkapsulacija ploščice popolna, pri notranji in zunanji ploščici pa je bilo opaziti znake razgradnje. Zaključimo lahko, da je bila potrjena sposobnost vsadka, da ohrani fiziološko funkcijo pri uporabi v obtočilih.

Družba Radi Medical System AB je v okviru načrta kliničnega razvoja za sistem FemoSeal™ VCS izvedla klinično raziskavo pred dajanjem na trg. Ta klinična raziskava ni objavljena in ni na voljo na spletu. Študija z modelom pripomočka št. 11200 je bila izvedena v letih 2002–2004 v skladu z evropskim standardom EN 540 (Klinične raziskave medicinskih pripomočkov za ljudi) in v skladu s smernicami ICH General Considerations for Clinical Trials in Guideline for Good Clinical Practice. Podrobnosti te študije so dokumentirane v poročilu EU-SE-001. Klinično preskušanje je bilo dokumentirano v končnem poročilu družbe Radi Medical Systems AB »Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures«. Klinična študija je bila izvedena s prvim modelom pripomočka FemoSeal™ št. 11200 in je bila osredotočena na varnost in učinkovitost vsadnih zapiralnih komponent. Edina razlika med prvim modelom št. 11200 in trenutnim modelom C11202 je v velikosti French, 6 Fr oziroma 7 Fr, ter izboljšanjem uvajalnem sistemu. Klinične koristi, predvidena uporaba, načela delovanja in surovine za vsadne zapiralne elemente, notranje tesnilo in zunanjo zaklepno ploščico ostajajo nespremenjeni.

Pripomoček je bil predviden za uporabo pri pacientih, pri katerih so bili opravljeni diagnostični srčni ali intervencijski posegi na srcu z uporabo femoralne arterije kot mesta pristopa. Cilj te študije je bil ugotoviti varnost, delovanje in učinkovitost sistema FemoSeal™ VCS. To je bila prospektivna, multicentrična, odprta študija z eno skupino in 30-dnevnim spremljanjem.

Primarna končna točka učinkovitosti je bil čas do hemostaze, opredeljen kot odsotnost pospešene krvavitve. Primarna končna točka varnosti je bila pojavnost večjih vaskularnih zapletov v 30 dneh. Sekundarne končne točke so vključevale čas do hoje, delež neuspešnih zdravljenj,

pogostnost neželenih dogodkov ter značilnosti učinkovitosti pripomočka med uvajanjem in namestitvijo.

V to študijo so bili vključeni odrasli pacienti, ki so lahko podali prostovoljno soglasje in so imeli vsaj en ohranjen pulz na nogah. Pacienti so bili izključeni iz študije, če so imeli katerega koli od naslednjih stanj:

- anamnezo periferne arterijske bolezni;
- avtoimunsko bolezen;
- znano motnjo krvavitve zaradi hude anemije;
- INR > 1,5;
- miokardni infarkt v 72 urah;
- nenadzorovano hipertenzijo kljub zdravljenju;
- debelost, ki preprečuje pristop s Seldingerjevo tehniko;
- prisotnost žilnega presadka ali stenta na mestu arteriotomije;
- predhodno ipsilateralno punkcijo v 3 mesecih;
- pričakovano življenjsko dobo < 6 mesecev.

Poleg tega so paciente pregledali intraoperativno in jih izključili iz študije, če so opazili kar koli od naslednjega:

- premer svetline skupne femoralne arterije < 5 mm;
- veje arterije znotraj 2 cm proksimalno od mesta punkcije;
- pomembno stenozo znotraj 3 cm od mesta punkcije;
- uporabo primarnega uvajalnega tulca velikosti > 6 Fr;
- punkcijo na femoralni bifurkaciji ali distalno od nje;
- več femoralnih punkcij;
- znana ali domnevna punkcija posteriorne stene femoralne arterije;
- velik hematoma (2 : 6 cm) ob zaključku posega;
- težave pri vstavljanju primarnega uvajala za poseg zaradi zvijuganega tkiva ali žile.

Ta študija z enim protokolom je bila izvedena v dveh delih: v 1. delu je bilo vključenih 20 pacientov, nato je bila opravljena analiza varnosti, v 2. delu pa je bilo vključenih dodatnih 60 pacientov.

V 1. delu je bila povprečna starost vključenih pacientov 65,9 leta, 70,0 % pacientov je bilo moškega spola in 95 % pacientov je prejelo sočasna zdravila. v 2. delu študije je bila povprečna starost 63,8 leta, 78 % je bilo moških in 100 % jih je prejelo sočasna zdravila.

V študijo so se lahko vključili pacienti z diagnostičnimi (1. in 2. del) ali intervencijskimi (2. del) posegi kateterizacije srca. Posegi so bili skladni s standardno oskrbo v vsaki od vključenih bolnišnic, čemur je sledila uporaba sistema FemoSeal™ VCS. Podatki o pacientih so bili zbrani ob izhodišču, med posegom ter 1 dan in 30 dni po posegu. Rezultati so povzeti v **preglednici 1.5** ter kažejo, da je sistem FemoSeal™ VCS varen in učinkovit za uporabo pri tej populaciji pacientov.

**Preglednica 1.5 Poročani klinični rezultati iz študije pred dajanjem na trg**

|                                                                                                         | 1. del      | 2. del                   |
|---------------------------------------------------------------------------------------------------------|-------------|--------------------------|
| Število pacientov                                                                                       | 20          | 60                       |
| Srednji čas do hemostaze                                                                                | 1,2 minute  | 1,6 minute <sup>a</sup>  |
| Srednji čas do hoje                                                                                     | 72,2 minute | 87,5 minute <sup>b</sup> |
| Pojavnost večjih vaskularnih zapletov <sup>c</sup>                                                      | 0 (0 %)     | 1 (2 %)                  |
| Število pacientov z neželenimi dogodki                                                                  | 5 (25 %)    | 19 (32 %)                |
| Neuspešno zdravljenje (opredeljeno kot večji vaskularni zapleti, potreba po ročni kompresiji ali oboje) | 0 (0 %)     | 3 (5 %)                  |
| Okvare pripomočka                                                                                       | 0 (0 %)     | 6 (10 %)                 |

<sup>a</sup>Na podlagi skupnega vzorca 58 pacientov, ker pri 2 pacientih v času posega ni bila dosežena hemostaza zaradi predhodnih ipsilateralnih punkcij. Pri teh pacientih je bila hemostaza dosežena po 7 minutah in 37 minutah.

<sup>b</sup>Na podlagi skupnega vzorca 59 pacientov: 1 pacient ni bil vključen, ker je bil zaradi pljučnega edema priključen na respirator in več kot teden dni ni mogel hoditi.

<sup>c</sup>Opredeljen kot vaskularni zaplet, ki zahteva transfuzijo krvi ali kirurško reparacijo, ali lokalna okužba, ki zahteva uporabo antibiotika, hospitalizacijo oziroma podaljšanje hospitalizacije ali nekrektomijo.

V 1. delu študije ni bilo opaziti večjih vaskularnih zapletov. v 2. delu študije so poročali o 1 večjem vaskularnem zapletu: psevdoanevrizmi, o kateri so poročali v 1 dnevu po posegu. Dogodek je zahteval ultrazvočno vodeno kompresijo in injiciranje trombina v psevdoanevrizmo ter je podaljšal pacientovo hospitalizacijo.

Od 5 neželenih dogodkov, o katerih so poročali v 1. delu študije, je bil 1 neželeni dogodek verjetno povezan s pripomočkom: nenevaren dogodek pospešene krvavitve 1 dan po posegu. Od 19 neželenih dogodkov, o katerih so poročali v 2. delu študije, so bili s pripomočkom povezani 3 nenevarni neželeni dogodki hematoma, 6 nenevarnih dogodkov pa je bilo verjetno povezanih s pripomočkom, vključno s 3 poročili o neprestanem izcedku, 2 hematomoma in 1 bolečino v nogi po vadbi.

V 2. delu zdravljenje ni bilo uspešno pri 3 pacientih: pri 2 zaradi nedoseganja hemostaze brez uporabe kompresije in pri 1 zaradi večjega vaskularnega zapleta (psevdoanevrizme). v 1. delu študije ni bilo primerov neuspešnega zdravljenja.

Od šestih okvar pripomočka v 2. delu študije tri niso ovirale posega, ena je bila posledica napake uporabnika, ena je bila posledica puščanja uvajala, do ene pa je prišlo zaradi zlomljenega filamentnega spoja. Zadnji dve težavi sta bili odpravljeni s posodobitvami modela, izvedenimi na modelu C11202.

V 2. delu klinične študije pred dajanjem na trg niso poročali o 6-mesečnih rezultatih spremljanja zaradi neskladnosti pacientov. Rezultati 30-dnevne klinične študije pred dajanjem na trg (EU-SE-001), ki so v skladu z obdobjem spremljanja iz klinične literature, dokazujejo, da je sistem FemoSeal™ VCS varen in učinkovit.

## 1.4.2 Povzetek podatkov iz kliničnih študij po dajanju na trg

V spodnji preglednici 1.6 so opisane 4 zaključene klinične študije po dajanju na trg. Te klinične raziskave niso objavljene in niso na voljo na spletu.

**Preglednica 1.6 Klinične študije po dajanju na trg**

| Zaključene klinične študije po dajanju na trg                                                              |                                    |                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                    |                                                                                                                                                     |
|------------------------------------------------------------------------------------------------------------|------------------------------------|---------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|
| Ime študije                                                                                                | Leto/<br>informacije o<br>podjetju | Vrsta študije                                                                         | Cilji                                                                                                                                                                                                                                                                                                                                                                                                                           | Mejniki                                                                                                                                                                                                                                                                                            | Možna merila<br>sprejemljivosti                                                                                                                     |
| PMS FemoSeal®<br>VCS #11202<br>(R1756-01) (2006)<br>User Acceptability<br>of New Packaging<br>(SIS) (2006) | 2006<br><br>RADI                   | Študija po<br>dajanju na trg,<br>uporabniška<br>sprejemljivost<br>novega<br>pakiranja | Študija po dajanju na trg,<br>izvedena s posodobljenim<br>modelom FemoSeal<br>Vascular® Closure System<br>št. 11202, ki ima spremenjen<br>uvajalni sistem v primerjavi<br>s prvim modelom št. 11200,<br>za dokumentiranje<br>funkcionalnosti.<br><br>Cilj študije je bil pridobiti<br>povratne informacije o<br>revidiranih navodilih za<br>uporabo in projektu<br>usposabljanja za zdravnike in<br>medicinske sestre, potrditi | 100 pacientov<br><ul style="list-style-type: none"> <li>63 moških/37 žensk</li> <li>Srednja starost 68 let za<br/>ženske, 65 let za moške</li> </ul> 2 švedski bolnišnici, 6<br>zdravnikov<br><br>112 pripomočkov<br><br>Podatki, zabeleženi v obrazcih za<br>zbiranje kliničnih podatkov<br>(CRF) | Rezultati<br><br>1. Ilustracije/navodila<br>v navodilih za uporabo veljajo<br>za informativne in ustrezne<br><br>2. Takojšnja hemostaza<br>(91/100) |

|                                                                                   |                                                               |                                     |                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
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|                                                                                   |                                                               |                                     | ocene iz analize tveganja ter prispevati k morebitnim izboljšavam kakovosti izdelka.                                                                                                                                                                                         | Predvideni čas opazovanja – 30 minut od časa uporabe                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008) | Dr. Nicolas Moes, Medicinska fakulteta v Innsbrucku, Avstrija | Potrditvena ocena po dajanju na trg | Cilj te študije je bil oceniti varnost in učinkovitost pripomočka FemoSeal®, pri običajni klinični uporabi pri pacientih, pri katerih je bila opravljena diagnostična kateterizacija srca ali intervencijski perkutani kirurški poseg na srcu, ki se izvaja z uvajalom 7 Fr. | 50 zaporednih pacientov<br><br>Indikacija – diagnostična ali invazivna kateterizacija srca iz skupne femoralne arterije<br><table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yr)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                                                                                                                         | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yr) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | Primarne končne točke <ul style="list-style-type: none"><li>Primarna končna točka učinkovitosti – čas do hemostaze z izcedkom ali brez, vendar brez dodatne ročne ali mehanske kompresije.</li><li>Končna točka varnosti – pojavnost neželenih dogodkov – manjših in večjih vaskularnih zapletov ter vseh drugih neželenih dogodkov – resnih in manj resnih v času trajanja študije (tj. do odpusta pacienta iz bolnišnice).</li></ul> Rezultati <ul style="list-style-type: none"><li>Srednji čas do hemostaze</li><li>Diagnostično – 56,6 ± 29 sekund</li><li>Intervencijsko – 59,9 ± 16,2 sekundi</li><li>Vsi pacienti – 57,8 ± 26,3</li><li>Vsi pacienti so po 4 urah počivanja v postelji hodili brez težav.</li></ul> Rezultati glede varnosti <ul style="list-style-type: none"><li>49/50 (98 %) brez vaskularnih zapletov do odpusta iz bolnišnice</li><li>Srednji čas do odpusta iz bolnišnice 2,6 dneva</li><li>Pri 1/50 (2 %) manjša krvavitev naslednji dan po nemoteni hoji na dan angiografije</li></ul> |
| n                                                                                 | 50                                                            |                                     |                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| men                                                                               | 35 (70%)                                                      |                                     |                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| women                                                                             | 15 (30%)                                                      |                                     |                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| PCI cases                                                                         | 15                                                            |                                     |                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| age (yr)                                                                          | 62.8±11.1                                                     |                                     |                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| body mass index (kg/m²)                                                           | 25.4±6.7                                                      |                                     |                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| systolic BP (mmHg)                                                                | 131.2±20.9                                                    |                                     |                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| diastolic BP (mmHg)                                                               | 77.9±10.6                                                     |                                     |                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| diabetes mellitus                                                                 | 9 (18%)                                                       |                                     |                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| arterial hypertension                                                             | 34 (68%)                                                      |                                     |                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| previous coronary intervention                                                    | 13 (26%)                                                      |                                     |                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| preprocedure aspirin                                                              | 50 (100%)                                                     |                                     |                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| preprocedure clopidogrel                                                          | 50 (100%)                                                     |                                     |                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Procedural unfractionated heparin                                                 | 15 (30%)                                                      |                                     |                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Procedural abciximab                                                              | 2 (4%)                                                        |                                     |                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                           |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)    | 2009 RADI                                                     | Študija po dajanju na trg           | Študija naj bi pokazala, ali so kupci/uporabniki zaznali kakršne koli težave z novim pakiranjem, zlasti z nesterilno zunanjo stranjo vrečke Tuvek/PET-PE.<br><br>Študija bi morala podati tudi informacije o tem, ali lečeči                                                 | 25 pripomočkov<br>4 švedske bolnišnice<br><br>16/25 (64 %) pacientov je bilo pacientov s PCI z močnimi antikoagulacijskimi zdravili                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Rezultati<br>1. Težave, povezane s pakiranjem – 21/25 (84 %) uporab je bilo uspešnih; 4/25 (16 %) je bilo neuspešnih (1 – testiranje novega uvajalnega tulca, 1 notranja ploščica je pri koraku izvleka prodrla skozi arteriotomijo, gumb |    |     |          |       |          |           |    |          |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |

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|----------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                        |                                        |                                                                          | <p>zdravnik opaža kakršne koli razlike pri uporabi/namestitvi pripomočka v primerjavi s predhodno uporabljenimi pripomočki.</p> <p>Študija bi morala prispevati tudi k opredelitvi morebitnih nadaljnjih potreb po izboljšanju kakovosti izdelka.</p> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | <p>se je dvignil in zunanja ploščica se je namestila v kanal reza v tkivo, 2 takojšnja hemostaza ni bila dosežena, čeprav ni bilo težav z namestitvijo.)</p> <p>2. Takojšnja hemostaza pri 19/25 (76 %) pacientov</p> <p>3. Krvavitev pri 11/25 (44 %) – pri 9/25 (36 %) izcedek/krvavitev, pri 2/25 (8 %) hematomi</p> <p>Skupna stopnja dogodkov: 19 %</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| <p>The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022)</p> | <p>2022/Terumo Medical Corporation</p> | <p>Prospektivna, multicentrična opazovalna študija po dajanju na trg</p> | <p>Dodatno dokazovanje varnosti in učinkovitosti sistema FemoSeal™ VCS pri doseganju hemostaze na mestu pristopa skozi skupno femoralno arterijo (CFA) pri resničnih udeležencih, pri katerih so opravili perkutane endovaskularne posege.</p>        | <ul style="list-style-type: none"> <li>Spremljanje pacienta po 30 dneh (<math>\pm 7</math> dni) z obiskom bolnišnice ali telefonskim klicem.</li> <li>Vključitev: od decembra 2021 do julija 2022.</li> <li>230 vključenih oseb, pri katerih so bili opravljeni diagnostični in intervencijski endovaskularni posegi z uporabo sistema FemoSeal™.</li> </ul> <p>3 lokacije v Evropi: Francija (92 pacientov), Nemčija (38 pacientov), Belgija (100 pacientov).</p> | <ul style="list-style-type: none"> <li><b>Demografski podatki/sočasne bolezni:</b> <ul style="list-style-type: none"> <li>- Spol: 161 moških (70 %)/69 žensk (30 %).</li> <li>- Povprečna starost: 70 <math>\pm 12</math>.</li> <li>- ITM: 26,1 <math>\pm</math> 4,95 kg/m<sup>2</sup>.</li> <li>- Hipertenzija: 160 pacientov (69,6 %).</li> <li>- Dislipidemija: 128 (55,7 %).</li> <li>- Koronarna arterijska bolezen: 42 (18,3 %).</li> <li>- Trenutni kadičci: 86 (37,6 %).</li> <li>- Nekdanji kadičci: 66 (28,8 %).</li> <li>- Koronarna srčna bolezen: 34 (14 %).</li> <li>- Miokardni infarkt v anamnezi: 18 (7,8 %).</li> <li>- Revaskularizacija periferne arterije: karotidna arterija 12 (5,2 %) in arterija spodnje okončine 83 (37,5 %).</li> <li>- Antiagregacijsko zdravljenje (ob izhodišču): 211 (91,7 %), vključno z 21 (9,1 %) z dvojnimi antiagregacijskim zdravljenjem (DAPT).</li> <li>- Peroralna antikoagulacija: 40 (17,4 %) pacientov.</li> </ul> </li> </ul> |

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|--|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <ul style="list-style-type: none"> <li>• <b>Značilnosti intervencijskega posega:</b> <ul style="list-style-type: none"> <li>- Okolje: bolnišnično – 162 primerov (70,4 %), ambulantno – 68 primerov (29,6 %).</li> <li>- Najpogostejša indikacija: klavdikacija – 147 primerov (63,9 %).</li> <li>- Pristop: 35 (15,3 %) – antegradni, 194 (84,7 %) – retrogradni.</li> </ul> </li> <li>• <b>Primarne končne točke:</b> <ul style="list-style-type: none"> <li>- Kombinirana končna točka varnosti (brez večjih zapletov na okončini na mestu pristopa v 6 urah po posegu) in učinkovitosti (uspešna hemostaza na mestu punkcije) je bila dosežena pri 215/226 (95,1 %) [95-% IZ: 91,46; 97,55] pacientov pri celotnem naboru pacientov za analizo in pri 215/230 (93,5 %) [95-% IZ: 89,47; 96,30] pacientov pri naboru pacientov, zdravljenih s pripomočkom FemoSeal™.</li> <li>- Končna točka učinkovitosti je bila dosežena pri 219/226 (96,9 %) [IZ: 93,7; 98,7] pacientov.</li> <li>- Končna točka varnosti je bila dosežena pri 220/230 (95,2 %) [95-% IZ: 92,15; 97,90] pacientov.</li> </ul> </li> <li>• <b>Sekundarne končne točke:</b> <ul style="list-style-type: none"> <li>- Odsotnost manjših zapletov na mestu pristopa v šestih urah po posegu je bila dosežena pri 225/230 (97,8 %) [95-% IZ: 95,00; 99,29] pacientov.</li> <li>- Odsotnost večjih in manjših zapletov na</li> </ul> </li> </ul> |
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|--|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <p>mestu pristopa od šestih ur do 30 dni po posegu je bila dosežena pri 219/230 (95,2 %) [95-% IZ: 91,60; 97,59] pacientov.</p> <p>- Srednji čas do hemostaze s pripomočkom FemoSeal™ VCD: 0,42 (0,25; 0,50) minute.</p> <p>- Srednji čas do hoje: 5,00 (4,54; 5,50) minut.</p> <p>- Mediana trajanja hospitalizacije: 23,98 (22,72; 25,00) ure.</p> <p>- Uporabnost sistema FemoSeal™ VCS: »preprosta« ali »zelo preprosta« namestitvev v 98,7 % primerov (»preprosta« namestitvev v 21 primerih (9,2 %), »zelo preprosta« namestitvev v 205 primerih (89,5 %)), brez upora ali z malo upora pri namestitvi v 226 primerih (98,3 %).</p> <p>Pri 152/230 (66,1 %) pacientov, zdravljenih z vodilno žico, ki je priložena kompletu FemoSeal™ (vodilna žica s premerom 0,038") in priporočena pri FemoSeal™, niso poročali o pomanjkljivostih pripomočka ali neželenih dogodkih.</p> |
|--|--|--|--|--|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Študija iz leta 2006 je bila izvedena za potrditev varnosti in učinkovitosti trenutnega pripomočka z izboljšanim uvajalnim sistemom ter pridobitev povratnih informacij o navodilih za uporabo sistema FemoSeal™ VCS in programu usposabljanja. v študijo je bilo vključenih 100 pacientov, primarna končna točka pa je bila, ali je bila dosežena hemostaza oziroma ali je bila potrebna dodatna ročna ali mehanska kompresija. v tej študiji je bilo ugotovljeno, da je bila uporaba sistema FemoSeal™ VCS uspešna v večini primerov (v 91 % je bila dosežena takojšnja hemostaza).

V študijo iz leta 2008 je bilo vključenih 50 pacientov za oceno varnosti in učinkovitosti sistema FemoSeal™ VCS pri običajni klinični uporabi pri pacientih, pri katerih je bila opravljena kateterizacija srca z uvajalom 7 Fr. Primarna končna točka študije je bilo zbrati podatke o času do hemostaze in času do hoje brez dodatne kompresije, ročne ali mehanske. Rezultati študije so



pokazali, da je bil srednji čas do hemostaze 57,8 sekunde in da so vsi pacienti po 4 urah počivanja v postelji hodili.

Namen študije iz leta 2009 je bil oceniti novo pakiranje sistema FemoSeal™ VCS. v študijo je bilo vključenih 25 pacientov. Primarna končna točka je bila ugotoviti, ali je uporabnik imel kakršne koli težave s pakiranjem. Uporabniki niso opazili nobenih težav v zvezi z novim pakiranjem sistema FemoSeal™ VCS. v tej študiji so zbirali tudi podatke o času do hemostaze.

Cilj študije iz leta 2022 je bil proaktivno zbiranje podatkov o varnosti in učinkovitosti sistema FemoSeal VCS pri doseganju hemostaze na mestih pristopa skozi skupno femoralno arterijo (CFA) pri resničnih udeležencih, pri katerih so opravili perkutane endovaskularne posege. v študijo je bilo vključenih 230 pacientov. Primarne končne točke za register so uspeh posega (tj. uspešna hemostaza na mestu punkcije) in zmanjšanje števila večjih zapletov (npr. poškodba žil, krvavitev, povezana z mestom pristopa, okužba na mestu pristopa, ponavljajoča se ročna kompresija in nova ipsilateralna akutna ishemija noge, povezana z mestom pristopa). Študija je pokazala, da sistem FemoSeal™ VCS dobro deluje v resničnem okolju in zagotavlja učinkovito hemostazo ter nizko stopnjo zapletov na mestu pristopa pri bolnikih, pri katerih so bili opravljeni periferni endovaskularni posegi. Dokazuje dobro učinkovitost s kratkim časom do hemostaze in dobrimi povratnimi informacijami uporabnikov o uporabnosti, zaradi česar je FemoSeal™ VCS dragocen pripomoček za zapiranje na mestu femoralnega pristopa.

### 1.4.3 Povzetek podatkov iz kliničnega spremljanja po dajanju na trg

#### 1.4.3.1 Zaključeno klinično spremljanje po dajanju na trg

Povzetek izvedenih dejavnosti kliničnega spremljanja po dajanju na trg je naveden v preglednici 1.7 spodaj.

**Preglednica 1.7. Dejavnosti kliničnega spremljanja po dajanju na trg**

| Izvedene dejavnosti kliničnega spremljanja po dajanju na trg              |                             |                                                             |                                                                                                                               |                                                                                                                                                  |                                                                                                                                                                                                                                                                         |
|---------------------------------------------------------------------------|-----------------------------|-------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Ime dejavnosti                                                            | Leto/informacije o podjetju | Vrsta študije                                               | Cilji                                                                                                                         | Mejniki                                                                                                                                          | Možna merila sprejemljivosti                                                                                                                                                                                                                                            |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021<br>TMC                 | Klinična anketa po dajanju na trg - visokokakovostna anketa | Anketa po dajanju na trg za zbiranje prospektivnih povratnih informacij v zvezi z uporabo žilnega zapirala FemoSeal™ Vascular | <ul style="list-style-type: none"> <li>120 primerov</li> <li>8 različnih zdravnikov z &gt; 5 let izkušenj</li> <li>Več držav v Evropi</li> </ul> | <p><b>Ocene pripomočkov na lestvici 1–5 – izjave v anketi</b></p> <ul style="list-style-type: none"> <li>Kriteriji sprejemljivosti <ul style="list-style-type: none"> <li>Ocene 3–5 se štejejo za ugodne</li> <li>Vse izjave morajo imeti ≥ 80 %</li> </ul> </li> </ul> |

| Izvedene dejavnosti kliničnega spremljanja po dajanju na trg        |          |                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|---------------------------------------------------------------------|----------|-------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                     |          |                                                             | Closure Device, ki se distribuira na trgih Evropske unije.                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                              | <p>pozitivnih povratnih informacij</p> <ul style="list-style-type: none"> <li>Rezultati <ul style="list-style-type: none"> <li>Ni prejete izjave v anketi &gt; 20 % neugodnih odgovorov</li> <li>Ni bilo pritožb glede izdelka</li> </ul> </li> </ul>                                                                                                                                                                                                                           |
| 20210298 – 0,035” and 0038” Guidewire Clinical Survey Report (2021) | 2021 TMC | Klinična anketa po dajanju na trg - visokokakovostna anketa | Anketa po dajanju na trg za zbiranje prospektivnih povratnih informacij v zvezi z uporabo 0,035-palčne vodilne žice, ki je priložena žilnemu zapiralu Angio-Seal™ VIP Vascular Closure Device (VCD) velikosti 6 Fr, in 0,038-palčne vodilne žice, ki je priložena pripomočku Angio-Seal™ VIP VCD velikosti 8 Fr in sistemu žilnega zapirala FemoSeal Vascular Closure System, ki se distribuira na trgih Evropske unije. | <ul style="list-style-type: none"> <li>Ankete za 0,035-palčno žico <ul style="list-style-type: none"> <li>106 anket</li> <li>64 zdravnikov</li> </ul> </li> <li>Ankete za 0,038-palčno žico <ul style="list-style-type: none"> <li>109 anket</li> <li>55 zdravnikov</li> </ul> </li> <li>12 retrospektivnih anket</li> </ul> | <p><b>Ocene pripomočkov na lestvici 1–5 – izjave v anketi</b></p> <ul style="list-style-type: none"> <li>Kriteriji sprejemljivosti <ul style="list-style-type: none"> <li>Ocene 3–5 se štejejo za ugodne</li> <li>Vse izjave morajo imeti ≥ 80 % pozitivnih povratnih informacij</li> </ul> </li> <li>Rezultati <ul style="list-style-type: none"> <li>Vse vodilne žice so prejele sprejemljive ocene</li> <li>Ni bilo predloženih pritožb glede izdelka</li> </ul> </li> </ul> |

| Izvedene dejavnosti kliničnega spremljanja po dajanju na trg                                                                                                                |                         |                                                                         |                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|-------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| FemoSeal™<br>Vascular<br>Closure<br>System<br>PMCF<br>Clinical<br>Survey<br>Report:<br>Addressing<br>Gaps<br>Identified in<br>CER-FS-<br>2021 and<br>CER-FS-<br>2022 (2023) | 2023–2024<br><br>TMC/TE | Klinična anketa<br>po dajanju na trg<br>-<br>visokokakovostna<br>anketa | Za prospektivno<br>zbiranje<br>povratnih<br>informacij<br>v zvezi<br>z uporabo<br>sistema<br>FemoSeal VCS<br>z vodilnimi<br>žicami, ki se<br>distribuirajo na<br>trgu EU. | <ul style="list-style-type: none"> <li>• 126 anket</li> <li>• 7 lokacij</li> <li>• 5 držav</li> <li>• 14. november 2023–<br/>11. junij 2024</li> <li>• Medicinska<br/>specializacija<br/>zdravnika: <ul style="list-style-type: none"> <li>○ vaskularna<br/>kirurgija</li> <li>○ interventna<br/>radiologija</li> <li>○ angiologija</li> </ul> </li> </ul> | <b>Ocene pripomočkov na lestvici<br/>do 5 – izjave v anketi</b> <ul style="list-style-type: none"> <li>• Kriteriji<br/>sprejemljivosti <ul style="list-style-type: none"> <li>○ Ocene 3–5 se<br/>štejejo za<br/>ugodne</li> <li>○ Vse izjave<br/>morajo imeti<br/>≥ 80 %<br/>pozitivnih<br/>povratnih<br/>informacij</li> <li>○ Če se v tej<br/>anketi<br/>pojavi<br/>neželeni<br/>dogodki,<br/>morajo biti<br/>tisti, ki so<br/>bili<br/>predvideni<br/>v okviru<br/>obvladovanja<br/>tveganja.</li> </ul> </li> <li>• Demografski podatki<br/>pacientov <ul style="list-style-type: none"> <li>○ Ženski spol:<br/>29,4 %<br/>(37/126)</li> <li>○ Moški spol<br/>69,8 %<br/>(88/126)</li> <li>○ Spol ni<br/>naveden: 0,8<br/>(1/126)</li> <li>○ Starost<br/>&gt; 75 let:<br/>31,7 %</li> </ul> </li> <li>• Rezultati <ul style="list-style-type: none"> <li>○ Vodilna žica,<br/>priložena<br/>sistemu<br/>FemoSeal™<br/>VCS:<br/>101/126<br/>(80,2 %).</li> </ul> </li> </ul> |

| Izvedene dejavnosti kliničnega spremljanja po dajanju na trg |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|--------------------------------------------------------------|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                              |  |  |  |  | <ul style="list-style-type: none"> <li>○ Trajanje posega (minute): 63,4 (36,6) (povprečje (SD)); 57,0 (36,0–81,0) (mediana (IQR))</li> <li>○ Vse ocene učinkovitosti sistema FemoSeal™ VCS so bile ugodne.</li> <li>○ Vse ocene vodilne žice, priložene sistemu FemoSeal™ VCS, so bile ugodne.</li> <li>○ En neželeni dogodek (0,8 %): ploščici sistema FemoSeal™ VCS nista bili pravilno poravnani, verjetno zaradi uporabe toge vodilne žice (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 palca), pri kateri je bila za doseganje hemostaze potrebna ročna kompresija.</li> </ul> |

Družba Terumo Medical Corporation je v trenutnem obdobju poročanja (od 1. septembra 2019 do 31. avgusta 2024) izvedla tri visokokakovostne uporabniške ankete med zdravniki.

V kliničnih anketah o pripomočku FemoSeal™ so bili zbrani proaktivni klinični podatki o varnosti in učinkovitosti sistema FemoSeal™ VCS med klinično uporabo. Anketa je vključevala vprašanja o celotnem pripomočku in pripadajočih dodatkih, vključno z 0,038-palčno vodilno žico, ter njihovih neposrednih interakcijah. v kliničnih anketah o vodilni žici so bili zbrani proaktivni klinični podatki o varnosti in učinkovitosti 0,038-palčne vodilne žice, priložene sistemu FemoSeal™ VCS, med klinično uporabo. Vprašanja v anketi so bila osredotočena zlasti na splošno uporabo vodilne žice, od vstavitve skozi žilno uvajalo v ožilje do odstranitve žice.

Sistem FemoSeal™ VCS in 0,038-palčna vodilna žica, priložena pripomočku, sta dobila vse sprejemljive ocene in za pripomoček je bilo predloženih šest (6) pritožb, za vodilno žico pa devet (9) poročil brez pritožb, in sicer na podlagi ocene pripomb, prejetih iz visokokakovostnih kliničnih anket. Obravnavane so bile tako pritožbe glede pripomočka FemoSeal kot tudi pritožbe glede vodilne žice in vse pritožbe so bile ocenjene v okviru postopka nadzora po dajanju na trg družbe Terumo. Ugotovljenih ni bilo nobenih novih tveganj ali stopenj tveganja.

V okviru dejavnosti PMCF je bila leta 2024 izvedena uporabniška anketa med zdravniki. Rezultati ankete so pokazali, da je bila ocena učinkovitosti in varnosti sistema FemoSeal™ VCS na splošno zelo ugodna. Dokazana je bila tudi združljivost z drugimi vodilnimi žicami, ki niso standardno priložene sistemu FemoSeal™ VCS.

#### **1.4.3.2 Tekoče/načrtovano klinično spremljanje po dajanju na trg**

TMC izvaja/načrtuje eno dejavnost kliničnega spremljanja po dajanju na trg. Izvedena bo klinična anketa za prospektivno zbiranje povratnih informacij v zvezi z uporabo vodilne žice s sistemom FemoSeal VCS, ki se distribuira na trgu EU. Anketa bo potekala med zdravniki za ugotavljanje, katere vodilne žice so uporabili med posegom. Namen te ankete je obravnavati vrzel, ki je bila ugotovljena zaradi pomanjkanja literature in komentarjev zunanjih pregledovalcev glede združljivosti sistema FemoSeal™ VCS z uporabo vodilnih žic drugih blagovnih znamk, ki niso blagovne znamke družbe Terumo. Povratne informacije vključujejo tehnične rezultate, klinično učinkovitost in varnost v zvezi z učinkovitostjo pripomočka pri uporabi skupaj z različnimi vodilnimi žicami.

#### **1.4.4 Povzetek podatkov iz sistematičnega pregleda literature**

Družba Terumo Medical Corporation izvaja sistematične preglede literature za zbiranje ter ocenjevanje podatkov o klinični varnosti in učinkovitosti iz objavljenih študij o sistemu FemoSeal™ VCS in/ali podobnih pripomočkih. Namen letnega pregleda objavljene literature je ugotavljanje prej neznanih neželenih učinkov, spremljanje znanih neželenih učinkov, prepoznavanje nastalih tveganj ter morebitnih sistematičnih zlorab ali neodobrene uporabe sistema FemoSeal™ VCS.

Pri zadnjem sistematičnem pregledu literature, ki je zajemal obdobje od 1. septembra 2019 do vključno 31. avgusta 2024, je bilo najdenih 29 objavljenih študij, ki so vsebovale podatke o klinični varnosti in učinkovitosti sistema FemoSeal™ VCS. v triindvajsetih referencah so poročali o odobreni uporabi sistema FemoSeal™ VCS, v devetih študijah pa so poročali o neodobreni uporabi. Na splošno pregled literature o študijah, specifičnih za uporabo sistema FemoSeal™ VCS kaže, da je preučevana populacija reprezentativna za paciente v EU, pri katerih so potrebni posegi perkutane žilne kateterizacije. Za seznam teh 23 strokovno pregledanih publikacij o odobreni uporabi glejte **Razdelek 3**.

Klinična učinkovitost je bila ocenjena po naslednjih merilih:

- Čas do hemostaze je boljši ali primerljiv z zadnjim stanjem tehničnega razvoja na področju perkutane zapiranja skupne femoralne arterije.
- Čas do hoje je boljši ali primerljiv z zadnjim stanjem tehničnega razvoja na področju perkutane zapiranja skupne femoralne arterije.
- Stopnja pooperativnih zapletov je primerljiva ali nižja od trenutnih standardov oskrbe.

Na podlagi teh kliničnih meril učinkovitosti so podatki iz tega pregleda literature pokazali, da se sistem FemoSeal™ VCS lahko uspešno uporablja za zaprtje femoralne arterijske punkcije (arteriotomije) pri pacientih, pri katerih je bila opravljena perkutana kateterizacija z uporabo žilnega uvajala 7 Fr ali manjšega. Popolna hemostaza je bila dosežena pri večini obravnavanih pacientov (79,65–100 %) in je bila povezana s srednjim časom do hemostaze 0,5 minute, povprečni čas do odpusta iz bolnišnice pa je bil 3 dni. 69,2–86,7 % pacientov je bilo sposobnih hoje 5 ur po zaprtju, povprečni pooperativni počitek v postelji pa je bil 349 minut. Pri 3,68–4 % primerov so opazili odpoved sistema FemoSeal™ VCS, pri 0,9–4,4 % posegov pa je bila potrebna dodatna ročna kompresija.

Klinična varnost je bila ocenjena na podlagi neželenih dogodkov, med katerimi so bili:

- krvavitev,
- hematoma,
- psevdoanevrizma,
- modrica,
- arteriovenska fistula,
- okužba,
- smrt.

Pri vsakem od teh neželenih dogodkov je bila stopnja pojavljanja, o kateri so poročali pri sistemu FemoSeal™ VCS v vključenih študijah, nižja ali primerljiva s tistimi, o katerih so poročali v preteklosti pri ročni kompresiji in drugih žilnih zapirilih.

Pri pregledu 10 poročil o primerih ni bilo ugotovljenih neželenih dogodkov, saj ni bilo ugotovljenih nobenih novih, nepredvidenih, nastajajočih ali nesprejemljivih tveganj.

Splošna učinkovitost uporabe sistema FemoSeal™ VCS pri diagnostični angiografiji ali intervencijskih posegih je odvisna od več dejavnikov, kot so: spol, starost, anatomija bolnika, sočasne bolezni, anatomska umestitev mesta punkcije, izkušnje kirurga, način namestitve pripomočka VCD, pooperativna nega ipd. Poleg tehnične uspešnosti, vključno z doseganjem hemostaze, sistem FemoSeal™ VCS v primerjavi z žilnim zaprtjem po punkciji femoralne arterije zagotavlja tudi klinične koristi, kot sta krajši čas do hemostaze in krajši čas do hoje. Rezultati o učinkovitosti sistema FemoSeal™ VCS so skladni s tistimi, ki so predvideni pri tej vrsti pripomočka, če se sistem uporablja v skladu s predvideno uporabo. Nekatere reference, pridobljene med trenutnim obdobjem iskanja, so pokazale uporabo zadevnega pripomočka na anatomske mestu, ki ni skupna femoralna arterija, in za zapiranje arteriotomij > 7 Fr, kar se šteje za neodobreno uporabo.

Med pregledom niso bili ugotovljeni nobeni neznani neželeni učinki, nastala tveganja ali možna sistematična zloraba pripomočka. Če sistem FemoSeal™ VCS previdno uporabljajo usposobljeni zdravniki, medicinski pripomoček deluje kot koristen in potreben klinični pripomoček. Na splošno ciljno zdravljenje in s tem sistem FemoSeal™ VCS izpolnjujeta klinično potrebo, ki trenutno obstaja pri zdravljenju zapletov, povezanih z žilnim pristopom.

Na splošno podatki iz tega pregleda literature niso pokazali nobenih predhodno neznanih težav z učinkovitostjo ali varnostjo pripomočka v kliničnem okolju ali neželenih učinkov, ki bi se pojavljali v večjem obsegu od pričakovanega/sprejemljivega. Zato lahko na podlagi tega pregleda literature sklepamo, da sistem FemoSeal™ VCS pri uporabi za kompresijo za doseganje hemostaze na mestu arteriotomije po perkutani kateterizaciji še naprej deluje po pričakovanih in ni povezan z resnimi dogodki varnosti.

#### **1.4.5 Povzetek podatkov iz nadzora po dajanju na trg**

Vzpostavljen je proaktivni sistem PMS, vse pritožbe pa so mesečno pregledane v skladu z internimi proizvodnimi postopki. Analizirani so bili podatki o pritožbah v časovnem obdobju od 1. septembra 2019 do 31. avgusta 2024. Skupno je bilo proizvajalcu predloženih 28 poročil o vigilanci medicinskih pripomočkov (MDV) in 476 poročil o pritožbah kupcev. Od 28 poročil o MDV je bilo 27 povezanih z neželenimi dogodki, eden pa z okvaro pripomočka. v obdobju poročanja sta bila dva primera s smrtnim izidom, vendar ni bilo presojeno, da je kateri od poročenih primerov s smrtnim izidom povezan z zadevnim pripomočkom. Med 476 pritožbami, naslovljenimi na proizvajalca, so bile najpogostejši razlog za pritožbe težave pri namestitvi (146 primerov, stopnja pojavljanja 0,0142 %). Druga najpogostejša vrsta okvare so dogodki izvleka s stopnjo 0,0126 % (130 dogodkov).

Sistem žilnega zapirala FemoSeal™ Vascular Closure System je bil prodan v več kot 1 030 136 primerkih po vsem svetu in 827 843 primerkih v Evropskem gospodarskem prostoru. Izračunana pogostost pritožb na podlagi globalne prodaje je 0,046 %. Skupna stopnja pritožb kupcev je zelo

nizka. Ugotovljena niso bila nobena nova tveganja, ki še ne bi bila vključena v navodila za uporabo in dokumentacijo o tveganjih.

Stopnje pojavljanja neželenih stranskih učinkov so prikazane v **preglednici 1.2.** v pritožbah ni bilo ugotovljenih nobenih novih nepričakovanih, nastajajočih ali nesprejemljivih tveganj. Ni bilo pomembnega povečanja pogostnosti ali resnosti znanih neželenih stranskih učinkov.

#### 1.4.6 Splošni povzetek o klinični učinkovitosti in varnosti

Sistem FemoSeal™ VCS je indiciran za uporabo pri zapiranju skupne femoralne arterijske punkcije (arteriotomije) pri pacientih, pri katerih je bila opravljena perkutana kateterizacija z uporabo žilnega uvajala 7 Fr (2,33 mm) ali manjšega. To klinično vrednotenje temelji na celoviti analizi razpoložljivih kliničnih podatkov in literature pred dajanjem na trg in po njem, ki so pomembni za predvideno uporabo sistema Femoseal™ VCS.

Celovit pregled objavljene literature je bil opravljen za obdobje od 1. septembra 2019 do vključno 31. avgusta 2024. Sklop dokazov je vključeval 29 študij za sistem FemoSeal™ VCS. Dokazi, navedeni v kliničnem vrednotenju, kažejo, da je zadevni pripomoček varen in učinkovit, če se uporablja v skladu z indikacijami, in da vsa tveganja ali neželeni stranski učinki, ki so lahko povezani s pripomočkom pri običajnih pogojih uporabe, predstavljajo sprejemljiva tveganja v primerjavi s koristmi za pacienta. Rezultati o učinkovitosti zadevnih pripomočkov so skladni s tistimi, ki so predvideni pri tej vrsti pripomočka, če se zadevni pripomočki uporabljajo v skladu s predvideno uporabo.

Možni neželeni stranski učinki, povezani z uporabo sistema FemoSeal™ VCS, vključujejo neželene dogodke, o katerih pogosto poročajo pri alternativnih načinih zapiranja arteriotomij, npr. krvavitev in hematov. Na splošno so stopnje pojavljanja neželenih dogodkov, o katerih so poročali pri uporabi sistema FemoSeal™ VCS, podobne tistim, o katerih so poročali pri ročni kompresiji in podobnih žilnih zapirilih. Zlasti pri krvavitvah in hematomih so stopnje pojavljanja, o katerih so poročali pri uporabi sistema FemoSeal™ VCS, nižje od tistih, o katerih so poročali pri podobnih žilnih zapirilih. Vsi neželeni dogodki, o katerih so poročali v objavljeni literaturi in pri nadzoru po dajanju na trg, so bili ugotovljeni že pred tem (glejte **razdelek 1.3**).

Obstoječi podatki o klinični varnosti in učinkovitosti sistema FemoSeal VCS kažejo, da koristi za paciente zaradi uporabe tega žilnega zapirala odtehtajo morebitna tveganja, če se pripomoček uporablja v skladu z navodili za uporabo.

Kot je navedeno v prejšnjih razdelkih zgoraj, podatki o sistemu FemoSeal™ VCS izkazujejo doslednost med podatki, povezanimi s pripomočkom v postopku vrednotenja (npr. uporaba pripomočka, rezultati glede varnosti, klinična učinkovitost in klinične koristi), ter podatki, povezanimi s prepoznanimi enakovrednimi pripomočki in podobnimi pripomočki, navedenimi pod »Zadnje stanje tehničnega razvoja«.

Pri medsebojni analizi podatkov glede varnosti ni bilo ugotovljenih nobenih vrzeli med:



- podatki, navedenimi pod »Zadnje stanje tehničnega razvoja«;
- podatki glede pripomočka v postopku vrednotenja;
- podatki, navedenimi v Dokumentaciji o upravljanju tveganja;
- podatki, navedenimi na oznaki in/ali v navodilih za uporabo (tj. obravnavana so preostala tveganja, o katerih je treba obvestiti uporabnika).

Klinična varnost je bila dokazana z nizko stopnjo zapletov, ugotovljeno v objavljeni strokovno pregledani klinični literaturi, v kliničnih študijah, ki jih je sponzorirala družba in ob pregledu podatkov po dajanju na trg, pri čemer tudi ni bilo umika s trga. Ugotovljenih ni bilo nobenih pomislekov glede učinkovitosti, pregledana literatura pa je navajala, da je uporaba sistema FemoSeal™ VCS skladna z uporabo, kakor jo je predvidel proizvajalec.

### 1.5 Možne diagnostične ali terapevtske alternative

Za doseganje hemostaze na mestu arteriotomije po žilni kateterizaciji se tradicionalno uporablja ročna kompresija. Ročna kompresija je povezana z dolgotrajno imobilizacijo pacienta (do 8 ur po posegu) ter s precejšnjim nelagodjem in podaljšano hospitalizacijo. Nedavni sistematični pregled je pokazal, da je srednji čas do dosežene hemostaze z ročno kompresijo znašal 20,8 minute.<sup>1</sup>

Alternativa ročni kompresiji so zunanji hemostatski pripomočki za mehansko kompresijo mesta arteriotomije. Ti pripomočki ne skrajšajo časa do hemostaze ali časa do hoje, temveč zmanjšajo potrebo po osebju, saj nadomestijo ročno kompresijo z mehansko kompresijo. Stopnja neželenih dogodkov, povezanih z mehansko kompresijo, je podobna kot pri ročni kompresiji.

Žilna zapirala, kot je FemoSeal™ VCS, so zasnovana za zapiranje arteriotomije. Njihov cilj je skrajšati čas do hemostaze in omogočiti zgodnejšo hojo. Pri nedavnem sistematičnem pregledu, ki je vključeval 13 na trgu dostopnih pripomočkov, je bilo ugotovljeno, da je srednji čas do dosežene hemostaze z žilnim zapiralom 5,4 minute. Srednji čas do hemostaze pri posameznih žilnih zapirilih je bil od 1 minute (FemoSeal™ VCS) do 14 minut, pri večini pripomočkov pa od 4 do 10 minut.<sup>1</sup>

Pogosto poročani neželeni dogodki, povezani z zapiranjem mesta arteriotomije z ročnimi kompresijami, zunanjimi hemostatičnimi pripomočki ali žilnimi zapirali, vključujejo hematoma, krvavitev na mestu pristopa, psevdoanevrizmo, arteriovensko fistulo in okužbo. Isti sistematični pregled (34 randomiziranih nadzorovanih preskušanj, pri 14 401 bolnikih) je pokazal, da so bile pogostnosti neželenih dogodkov pri ročni kompresiji in uporabi žilnih zapiral podobne, razen da so bile pri žilnih zapirilih krvavitve nekoliko pogostejše.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Predlagani profil uporabnika in usposabljanje

Predvideni uporabniki sistema žilnega zapirala FemoSeal™ Vascular Closure System so zdravniki, ki so usposobljeni za izvajanje arterijskega pristopa in zapiranja pri endovaskularnih posegih skozi skupno femoralno arterijo in so se udeležili programa usposabljanja zdravnikov za uporabo pripomočkov FemoSeal™ družbe Terumo Medical Corporation.

## 1.7 Ustrezni usklajeni in skupni standardi

| Sklic na standard | Trenutno leto skladnosti/rev. | Opis                                                                                                                                     |
|-------------------|-------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070         | 2014/AMD1:2018                | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070      | 2014/A1:2018                  | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance      | 20. maj 2021                  | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052        | 2015                          | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213        | 2017                          | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503        | 2020                          | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182        | 2019                          | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |
| EN ISO 13485      | 2016/A11:2021                 | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 13485         | 2016                          | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |

| Sklic na standard | Trenutno leto skladnosti/rev. | Opis                                                                                                                                                                     |
|-------------------|-------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14644-1       | 2015                          | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1    | 2015                          | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2       | 2015                          | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2    | 2015                          | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3       | 2019                          | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3    | 2019                          | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1       | 2003                          | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1    | 2003                          | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2       | 2003/TC1:2004                 | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| EN ISO 14698-2    | 2003/TC 1:2004                | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| USP <788>         | n/r                           | PARTICULATE MATTER IN INJECTIONS                                                                                                                                         |

| Sklic na standard      | Trenutno leto skladnosti/rev. | Opis                                                                                                                 |
|------------------------|-------------------------------|----------------------------------------------------------------------------------------------------------------------|
| EU Pharmacopeia 2.9.19 | n/r                           | Particulate Contamination: Sub-Visible Particles                                                                     |
| IEC 62366-1            | 2015                          | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN 62366-1             | 2015                          | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN ISO 14971           | 2019/A11:2021                 | Medical devices — Application of risk management to Medical devices                                                  |
| ISO 14971              | 2019                          | Medical devices — Application of risk management to Medical devices                                                  |
| ASTM F1980             | 2016                          | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1         | 2020                          | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1            | 2018                          | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2         | 2006                          | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2            | 2006                          | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3         | 2014                          | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3            | 2014                          | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4         | 2017                          | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4            | 2017                          | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |

| Sklic na standard | Trenutno leto skladnosti/rev. | Opis                                                                                                                                       |
|-------------------|-------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-5    | 2009                          | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                                         |
| ISO 10993-5       | 2009                          | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                                         |
| EN ISO 10993-6    | 2016                          | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| ISO 10993-6       | 2016                          | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| EN ISO 10993-10   | 2023                          | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| ISO 10993-10      | 2021                          | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| EN ISO 10993-11   | 2018                          | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| ISO 10993-11      | 2017                          | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| EN ISO 10993-12   | 2021                          | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| ISO 10993-12      | 2021                          | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| EN ISO 10993-17   | 2009                          | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17      | 2002                          | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18      | 2020/A1:2022                  | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |

| Sklic na standard | Trenutno leto skladnosti/rev. | Opis                                                                                                                                                                         |
|-------------------|-------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-18   | 2020/A1:2022                  | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-23   | 2021                          | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23      | 2021                          | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382        | 2018                          | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756         | 2017                          | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>          | n/r                           | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>         | n/r                           | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72    | 2019                          | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135      | 2014/A1:2019                  | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135         | 2014/A1:2018                  | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7    | 2008/A1:2022                  | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |

| Sklic na standard | Trenutno leto skladnosti/rev. | Opis                                                                                                                                                            |
|-------------------|-------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-7       | 2008/A1:2019                  | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                               |
| EN 556-1          | 2024                          | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices |
| EN ISO 11737-1    | 2018/A1:2021                  | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11737-1       | 2018/A1:2021                  | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| EN ISO 11138-1    | 2017                          | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-1       | 2017                          | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| EN ISO 11138-2    | 2017                          | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 11138-2       | 2017                          | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| EN ISO 15223-1    | 2016                          | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| ISO 15223-1       | 2016                          | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| EN 1041           | 2008/A1:2013                  | Information supplied by the manufacturer of medical devices                                                                                                     |
| EN ISO 11607-1    | 2020/A1:2023                  | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                         |

| Sklic na standard | Trenutno leto skladnosti/rev. | Opis                                                                                                                                                                       |
|-------------------|-------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11607-1       | 2019/A1:2023                  | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| EN ISO 11607-2    | 2020/A1:2023                  | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ISO 11607-2       | 2019/A1:2023                  | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169        | 2016                          | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M | 2016                          | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825        | 2018                          | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096        | 2011 (R 2019)                 | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M     | 2015                          | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24      | 2021                          | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3       | 2020                          | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |
| MDCG 2020-8       | 2020                          | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                             |
| MDCG 2020-7       | 2020                          | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                          |



| Sklic na standard | Trenutno leto skladnosti/rev. | Opis                                                                                                                                                                                                                                                          |
|-------------------|-------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-6       | 2020                          | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                                                                                                          |
| MDCG 2019-9 v1    | 2022                          | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                                                                                      |
| MDCG 2019-8 v2    | 2020                          | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15      | 2020                          | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11      | 2021                          | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19      | 2021                          | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4    | 2021                          | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2       | 2019                          | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1       | 2019                          | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7       | 2018                          | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6       | 2018                          | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |

| Sklic na standard      | Trenutno leto skladnosti/rev. | Opis                                                                                                                                                                                          |
|------------------------|-------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2018-4            | 2018                          | MDCG 2018-4 Annex: UDI database<br>Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                               |
| MDCG 2018-3 v1         | 2020                          | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25           | 2021                          | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2.12-2<br>Rev 2 | 2012                          | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                        |

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### 3.0 ZGODOVINA REVIZIJ

| Številka revizije<br>SSCP    | Datum izdaje    | Opis sprememb                                                                       | Revizijo potrdil priglašeni<br>organ                                                                                                                                                                                                                                                                                                                                 |
|------------------------------|-----------------|-------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022                 | 20. januar 2023 | Prva izdaja, ob<br>certificiranju za<br>pridobitev oznake CE<br>v skladu z MDR      | <p><input checked="" type="checkbox"/> Da</p> <p>Jezik potrjevanja: English</p> <p><input type="checkbox"/> Ne (velja samo za vsadne<br/>pripomočke razreda IIa ali<br/>nekatero vsadne pripomočke<br/>razreda IIb (MDR, člen 52 (4),<br/>2. odstavek), za katere<br/>priglašeni organ še ni potrdil<br/>SSCP)</p> <p><input type="checkbox"/> Drugo (navedite):</p> |
| SSCP-FS-2023 –<br>revizija 1 | 15. marec 2024  | Posodobljeno za obdobje<br>od 1. januarja 2019 do<br>vključno<br>31. decembra 2023. | <p><input checked="" type="checkbox"/> Da</p> <p>Jezik potrjevanja: English</p> <p><input type="checkbox"/> Ne (velja samo za vsadne<br/>pripomočke razreda IIa ali<br/>nekatero vsadne pripomočke<br/>razreda IIb (MDR, člen 52(4),<br/>2. odstavek), za katere<br/>priglašeni organ še ni potrdil<br/>SSCP)</p> <p><input type="checkbox"/> Drugo (navedite):</p>  |
| SSCP-FS-2024<br>Revizija 1   |                 | Posodobljeno za obdobje<br>od 1. septembra 2019 do<br>vključno<br>31. avgusta 2024. | <p><input type="checkbox"/> Da</p> <p>Jezik potrjevanja: English</p> <p><input type="checkbox"/> Ne (velja samo za vsadne<br/>pripomočke razreda IIa ali<br/>nekatero vsadne pripomočke<br/>razreda IIb (MDR, člen 52(4),<br/>2. odstavek), za katere<br/>priglašeni organ še ni potrdil<br/>SSCP)</p> <p><input type="checkbox"/> Drugo (navedite):</p>             |

|                            |               |                                                          |                                                                                                                                                                                                                                                                                                                                                    |
|----------------------------|---------------|----------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>Revizija 2 | June 20, 2025 | Revidirano na podlagi<br>poizvedb NSAI za<br>potrjevanje | <input checked="" type="checkbox"/> Da<br>Jezik potrjevanja: English<br><br><input type="checkbox"/> Ne (velja samo za vsadne<br>pripomočke razreda IIa ali<br>nekatero vsadne pripomočke<br>razreda IIb (MDR, člen 52(4),<br>2. odstavek), za katere<br>priglašeni organ še ni potrdil<br>SSCP)<br><br><input type="checkbox"/> Drugo (navedite): |
|----------------------------|---------------|----------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

## Rezime bezbednosti i kliničkih performansi

### FemoSeal™ Vascular Closure System

|                                                              |                                                                                              |
|--------------------------------------------------------------|----------------------------------------------------------------------------------------------|
| <b>Proizvođač</b>                                            | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 USA          |
| <b>SRN proizvođača</b>                                       | US-MF-000019594                                                                              |
| <b>Predstavnik uprave / PRRC</b>                             | Kimberly Feitl<br>Vice President, Quality                                                    |
| <b>Osnovni UDI-DI</b>                                        | 38970FS79                                                                                    |
| <b>EMDN broj</b>                                             | C900199 – sistemi za hemostazu – drugo                                                       |
| <b>Klasa sredstva</b>                                        | Klasa III                                                                                    |
| <b>Godina kada je sredstvo prvi put<br/>dobilo CE oznaku</b> | 2005                                                                                         |
| <b>Predstavnik za EU</b>                                     | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgium<br>SRN: BE-AR-000001433 |
| <b>Notifikovano telo</b>                                     | NSAI<br>CE 0050                                                                              |



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Ovaj Rezime bezbednosti i kliničkih performansi (SSCP) treba da pruži javni pristup ažuriranom sažetku glavnih aspekata bezbednosti i kliničkih performansi sredstva FemoSeal™ Vascular Closure System (VCS).

Rezime bezbednosti i kliničkih performansi sredstva, namenjen korisnicima / zdravstvenim radnicima, dat je u nastavku u **odeljku 1.0**.

## **1.0 REZIME ZA KORISNIKE / ZDRAVSTVENE RADNIKE**

Nije predviđeno da SCP zameni Uputstvo za upotrebu kao glavni dokument koji će osigurati bezbednu upotrebu sredstva niti je predviđeno da pruži dijagnostičke i terapijske sugestije predviđenim korisnicima ili pacijentima. Nije predviđeno da SSCP zameni obavezne informacije na karticama za implantat ili bilo koje druge obavezne dokumente.

### **1.1 Namena sredstva**

#### **1.1.1 Namena**

FemoSeal™ Vascular Closure System je medicinsko sredstvo namenjeno za zatvaranje arterijske punkcije nakon perkutane kateterizacije kroz zajedničku femoralnu arteriju.

#### **1.1.2 Indikacije za upotrebu**

FemoSeal™ Vascular Closure System je indikovano za upotrebu u zatvaranju punkcije zajedničke femoralne arterije (arteriotomije) kod pacijenata koji su podvrgnuti perkutanoj kateterizaciji sa košuljicom za sprovođenje procedure ne većom od 7 F (2,33 mm).

#### **1.1.3 Kontraindikacije i/ili ograničenja**

FemoSeal™ Vascular Closure System je kontraindikovano kod pacijenata sa arteriotomijama kod koji se koriste košuljice ili sredstva veći od 7 F (2,33 mm).

#### **1.1.4 Ciljne populacije pacijenata**

Bezbednost i delotvornost sredstva FemoSeal™ Vascular Closure System utvrđene su kod pacijenata od najmanje 18 godina starosti koji su podvrgnuti perkutanoj kateterizaciji sa košuljicom za sprovođenje procedure ne većom od 7 F (2,33 mm).

#### **1.1.5 Posebne populacije pacijenata**

Bezbednost i delotvornost sredstva FemoSeal™ Vascular Closure System nisu utvrđene kod sledećih populacija pacijenata:

- Pacijenti sa postojećim autoimunim oboljenjem.
- Pacijenti koji su podvrgnuti terapijskoj trombolizi.
- Pacijenti sa klinički značajnim perifernim vaskularnim oboljenjem.
- Pacijenti sa hipertenzijom (> 220 mmHg sistolni ili > 110 mmHg dijastolni) koja nije pod kontrolom.
- Pacijenti sa poremećajem krvarenja, uključujući trombocitopeniju (< 100.000 trombocita) ili anemiju (Hgb < 10 mg/dl).

- Pacijenti koji imaju unutrašnji lumen zajedničke femoralne arterije manji od 5 mm.
- Pacijenti sa renalnom i/ili hepatičnom insuficijencijom.
- Pacijenti sa drugim relevantnim komorbiditetom.
- Populacija specifičnog rasnog i/ili etničkog porekla.
- Pacijenti sa infarktom miokarda u periodu od 72 sata.
- Pacijenti sa vaskularnim graftom ili stentom na mestu punkcije.
- Pacijenti u drugom stanju ili laktaciji.
- Pacijenti mlađi od 18 godina.

### 1.1.6 Predviđeni korisnici

Predviđeni korisnici sredstva FemoSeal™ Vascular Closure System su lekari sa obukom koja ih kvalifikuje za izvođenje arterijskog pristupa i zatvaranja kod endovaskularnih procedura preko zajedničke femoralne arterije i koji učestvuju u programu za obuku lekara za FemoSeal™ kompanije Terumo Medical Corporation.

## 1.2 Opis sredstva

### 1.2.1 Opis sredstva

FemoSeal™ Vascular Closure System, koji proizvodi kompanija Terumo Medical Corporation (TMC), je resorptivno vaskularno sredstvo za zatvaranje dizajnirano za postizanje hemostaze femoralne arterije nakon perkutane kateterizacije kroz zajedničku femoralnu arteriju.

FemoSeal™ elementi za zatvaranje sastoje se od dva resorptivna polimerna diska, unutrašnje zaptivke i spoljašnjeg diska za fiksiranje, koje spaja resorptivni multifilament čime se arteriotomija zatvara mehanički (pogledajte **sliku 1.1** i **sliku 1.2**). Nakon postavljanja kroz košuljicu konusnog kućišta, spoljašnji disk za fiksiranje se potiskuje na multifilamentnu osovinicu što dovodi do mehaničkog zatvaranja mesta punkcije između unutrašnjeg i spoljašnjeg diska za fiksiranje. Unutrašnju zaptivku i spoljni disk za fiksiranje na mestu drži frikcija na multifilamentnoj osovinici. Hemostaza se postiže mehaničkim sredstvima. Elementi za zatvaranje se razgrađuju hidrolizom.

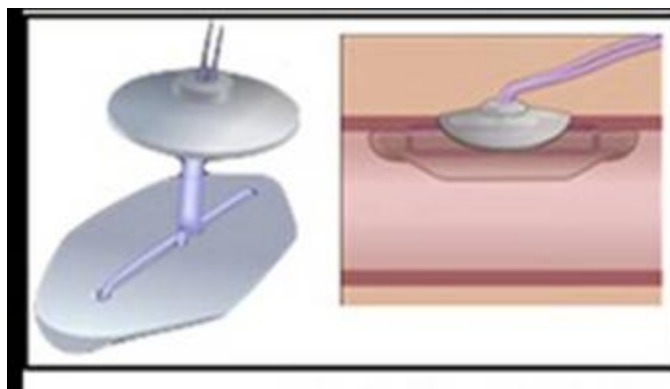
Implantabilne komponente za zatvaranje, unutrašnja zaptivka i spoljašnji disk za fiksiranje razgrađuju se u roku od osamnaest (18) meseci, dok se procenjuje da okolno tkivo razgrađuje i resorbuje multifilament nakon dve (2) do tri (3) godine. Sposobnost implantabilnih komponenta za zatvaranje da održe kompresiju na arteriotomiji je ispitana na najviše osam (8) sati. Proizvodi razgradnje se metabolišu i izlučuju kroz urin ili izbacuju kao ugljen-dioksid preko pluća. U

studijama na životinjama nisu uočeni efekti akumulacije. Dodatne komponente sredstva FemoSeal™ koje će doći u kontakt sa živim tkivom ili krvlju u toku procedure su košuljica konusnog kućišta, dilatator, cevčica za potiskivanje, potiskivač i žica vodič.

**Slika 1.1 Unutrašnja zaptivka i spoljašnji disk za fiksiranje, sleva nadesno**

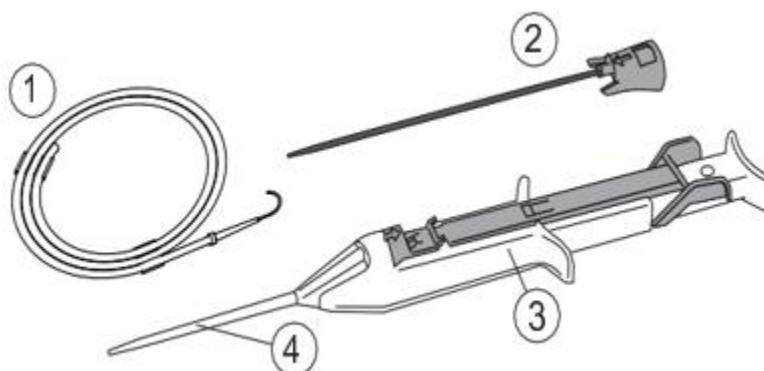


**Slika 1.2 Postavljeni unutrašnja zaptivka i spoljašnji disk**



FemoSeal™ jedinica se pakuje zajedno sa dilatatorom i žicom vodičem spoljašnjeg prečnika 0,038" (0,97 mm), dužine 27,5" (70 cm) i ispravljačem J-oblika, videti **sliku 1.3** u nastavku. Žica vodič se nalazi u polietilenskoj cevčici. Svi delovi su upakovani na fiksnoj papirnoj tacni. Pakovanje takođe sadrži karticu za implantat za pacijenta. FemoSeal™ Vascular Closure System ne zahteva dodatni pribor da bi sredstvo funkcionisalo kao što je predviđeno i sredstvo je namenjeno samo za upotrebu sa dilatatorom i žicom vodičem koji su priloženi u pakovanju proizvoda.

**Slika 1.3 FemoSeal™ VCS jedinica sa žicom vodičem i dilatatorom**



### 1.2.2 Sirovine i komponente

**Tabela 1.1** u nastavku navodi komponente sredstva FemoSeal™ VCS.

**Tabela 1.1 FemoSeal™ VCS sirovine i komponente**

| Broj dela | Opis                                                                |                                                                       | Materijali                                                                                                                                                                    |
|-----------|---------------------------------------------------------------------|-----------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1         | Žica vodič sa ispravljačem žice vodiča J-oblika od 0,038" (0,97 mm) |                                                                       | Žica vodič: 304 nerđajući čelik<br>Ispravljač J-oblika: polipropilen, ljubičasti pigment<br>Kopča: polietilen<br>Cevčice: polietilen                                          |
| 2         | FemoSeal dilatator                                                  |                                                                       | Čvorište: tetrahidrofur, plavi pigment, polibutilen-tereftalat (PBT)<br><br>Cevčica: polietilen velike gustine (HDPE), crni pigment<br><br>Lubrikant: silikon Dow Corning 360 |
| 3/4       | FemoSeal jedinica                                                   | Ukalupljen RD7 – unutrašnja zaptivka i spoljašnji disk za fiksiranje* | kopolimer glikolida, trimetilen-karbonata, ε-kaprolaktona i TMP: trimetilolpropan (inicijator)                                                                                |
|           |                                                                     | Multifilament *                                                       | segmentirani kopolimer L,L-laktida, trimetilen-karbonata, ε-kaprolaktona i 1,3 propanediola (inicijator)<br><br>Sloj je kopolimer glikolida, ε-kaprolaktona i L-lizina        |

|  |  |                            |                                                 |
|--|--|----------------------------|-------------------------------------------------|
|  |  | Cevčica za potiskivanje    | polipropilen                                    |
|  |  | Potiskivač                 | 304V nerđajući čelik                            |
|  |  | Klizač                     | polibutilen-tereftalat (PBT)                    |
|  |  | Kućište                    | polibutilen-tereftalat (PBT)                    |
|  |  | Dugme                      | polibutilen-tereftalat (PBT)                    |
|  |  | Poklopac dugmeta           | Polioksimetilen (POM) / poliacetalni kopolimer  |
|  |  | Rukavac                    | polibutilen-tereftalat (PBT)                    |
|  |  | Odstojnik                  | polibutilen-tereftalat (PBT)                    |
|  |  | Konus                      | polipropilen                                    |
|  |  | Poklopac kućišta           | polibutilen-tereftalat (PBT)                    |
|  |  | Sigurnosni jezičak         | polibutilen-tereftalat (PBT), plavi pigment     |
|  |  | Poklopac rukavca           | polibutilen-tereftalat (PBT)                    |
|  |  | Zaptivka cevčice           | silikon A 70 po Šoru                            |
|  |  | Zaptivka kućišta           | silikon A 50 po Šoru                            |
|  |  | Opruga                     | 302 nerđajući čelik                             |
|  |  | Košuljica konusnog kućišta | polipropilen<br>Silikon Dow Corning 360, heksan |

\* Implantabilan deo sredstva; implantabilne komponente su bezbedne za MR snimanje

FemoSeal™ VCS se sterilise etilen-oksidiom (EO) i predstavlja medicinsko sredstvo za jednokratnu upotrebu. FemoSeal™ VCS sredstvo je dizajnirano tako da ne može da se koristi više puta.

### **Način delovanja**

FemoSeal™ VCS unapređuje mehaničku hemostazu razvijanjem implantabilnih elemenata za zatvaranje unutar i izvan zajedničke femoralne arterije. Unutrašnja zaptivka koja zaptiva mesto punkcije i spoljašnji disk za fiksiranje koji drži unutrašnju zaptivku na mestu obezbeđuju mehanizam koji sprečava krvarenje.

### **1.2.3 Klinička korist**

FemoSeal™ VCS pruža sledeće kliničke koristi u pogledu vaskularnog zatvaranja nakon punkcije zajedničke femoralne arterije:



- Skraćeno vreme do hemostaze<sup>1</sup>
- Skraćeno vreme do ambulacije<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

#### 1.2.4 Prethodna generacija/generacije ili varijante

- Prva verzija FemoSeal™ VCS (br. 11200) prodavala se na evropskom tržištu u toku 2005. godine i delu 2006.
- Aktuelna verzija FemoSeal™ VCS (br. 11202), sa unapređenim sistemom dovoda, na tržištu je od 28. marta 2006. godine.

#### 1.2.5 Dodatni pribor predviđen za upotrebu u kombinaciji sa sredstvom

FemoSeal™ jedinica se pakuje zajedno sa dilatatorom, žicom vodičem spoljašnjeg prečnika 0,038" (0,97 mm), dužine 27,5" (70 cm) i ispravljačem J-oblika. Žica vodič je dodatni pribor jedinice FemoSeal™. Ispravljač J-oblika je komponenta žice vodiča, dok je dilatator komponenta jedinice FemoSeal™. Žica vodič je jedini dodatni pribor koji se razmatra. Žica vodič se nalazi u polietilenskoj cevčici. Svi delovi su upakovani na fiksnoj papirnoj tacni. Pakovanje takođe sadrži karticu za implantat za pacijenta. FemoSeal™ Vascular Closure System ne zahteva dodatni pribor da bi sredstvo funkcionisalo kao što je predviđeno i sredstvo je namenjeno samo za upotrebu sa dilatatorom i žicom vodičem koji su priloženi u pakovanju proizvoda.

#### 1.2.6 Druga sredstva i proizvodi predviđeni za upotrebu u kombinaciji sa sredstvom

Sredstvo FemoSeal™ VCS ne zahteva dodatna sredstva da bi funkcionisalo kao što je predviđeno.

### 1.3 Rizici i upozorenja

#### 1.3.1 Rezidualni rizici i neželjena dejstva

Poznati ili predvidivi neželjeni događaji, povrede i komplikacije koji se povezuju sa upotrebom sredstva FemoSeal™ VCS kao posledica rezidualnog rizika navedeni su u **tabeli 1.2**. Stopa javljanja je zasnovana na analizi dokumentacije o rizicima i izračunata na osnovu podataka o praćenju nakon plasiranja na tržište od 1. septembra 2019. godine do 31. avgusta 2024. godine. Nema nepoznatih rezidualnih rizika za FemoSeal™ VCS i svi primenljivi rizici su razmatrani kroz Uputstvo za upotrebu i proces upravljanja rizicima.

**Tabela 1.2. FemoSeal neželjeni događaji / komplikacije**

| Šteta                                               | Stopa javljanja (%) | Ublažujući faktori                                                                                                                          |
|-----------------------------------------------------|---------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| Alergijska reakcija                                 | 0,0000              | Mere i planovi za što veće smanjenje rizika rešeni su kroz dizajn proizvoda, smernice za proizvodnju, označavanje proizvoda i obuku lekara. |
| Aneurizma                                           | 0,0000              |                                                                                                                                             |
| AV fistula                                          | 0,0001              |                                                                                                                                             |
| Gubitak krvi / krvarenje                            | 0,0280              |                                                                                                                                             |
| Smrt                                                | 0,0002              |                                                                                                                                             |
| Ehimoza                                             | 0,0000              |                                                                                                                                             |
| Embolija                                            | 0,0000              |                                                                                                                                             |
| Reakcija na strano telo                             | 0,0000              |                                                                                                                                             |
| Hematom                                             | 0,0027              |                                                                                                                                             |
| Krvarenje                                           | 0,0001              |                                                                                                                                             |
| Infekcija                                           | 0,0002              |                                                                                                                                             |
| Inflamatorna reakcija                               | 0,0000              |                                                                                                                                             |
| Utrnulost                                           | 0,0000              |                                                                                                                                             |
| Bol                                                 | 0,0000              |                                                                                                                                             |
| Nelagodan osećaj kod pacijenta                      | 0,0004              |                                                                                                                                             |
| Odlaganje procedure                                 | 0,0065              |                                                                                                                                             |
| Pseudoaneurizma                                     | 0,0004              |                                                                                                                                             |
| Retroperitonealno krvarenje                         | 0,0002              |                                                                                                                                             |
| Sepsa                                               | 0,0000              |                                                                                                                                             |
| Tromboembolija                                      | 0,0000              |                                                                                                                                             |
| Tromboza                                            | 0,0001              |                                                                                                                                             |
| Okluzija krvnog suda / ishemija donjeg ekstremiteta | 0,0002              |                                                                                                                                             |
| Perforacija krvnog suda                             | 0,0000              |                                                                                                                                             |
| Disekcija/laceracija tkiva krvnog suda              | 0,0003              |                                                                                                                                             |

### 1.3.2 Upozorenja i mere predostrožnosti

#### Upozorenja

1. Nemojte koristiti ako je pakovanje oštećeno ili ako sterilna barijera nije očuvana.
2. Nemojte koristiti nakon isteka roka upotrebe – biorazgradive komponente možda neće imati adekvatan učinak.
3. Nemojte koristiti ako bilo koji elementi deluju oštećeno ili neispravno na bilo koji način.
4. Upotreba sredstva FemoSeal™ Vascular Closure System na mestu na kome je možda došlo do bakterijske kontaminacije košuljice za obavljanje procedure ili okolnog tkiva može izazvati infekciju.
5. Ako postoji sumnja da je posteriorni zid arterije probušen ili da je napravljeno više arterijskih punkcija, nemojte se oslanjati isključivo na FemoSeal™ Vascular Closure System za postizanje arterijske hemostaze. Primenite dodatnu ručnu ili mehaničku kompresiju.
6. Ako je mesto punkcije na bifurkaciji ili distalno u odnosu na bifurkaciju femoralne arterije, FemoSeal™ Vascular Closure System ne treba koristiti zbog rizika od nepravilnog pozicioniranja unutrašnje zaptivke. To može dovesti do komplikacija sa krvarenjem i/ili disrupcije normalnog protoka krvi.
7. Ako postoji uporno arterijsko krvarenje na mestu reza, ne secite multifilament dok se ne postigne hemostaza. Ako se hemostaza ne postigne, pričvrstite multifilament sterilnom kompresom i primenite dopunsku kompresiju dok se ne postigne hemostaza. U slučaju upornog arterijskog krvarenja, mogu da se jave značajne komplikacije sa krvarenjem što može da dovede do povrede ili smrti pacijenta.
8. Nemojte koristiti FemoSeal™ Vascular Closure System ako je mesto punkcije proksimalno u odnosu na ingvinalni ligament, jer ovo može da dovede do retroperitonealnog hematoma.
9. Pacijenti sa povišenim rizikom od krvarenja mogu da pretrpe povećan gubitak krvi koji zahteva transfuziju.
10. Ako se unutrašnji disk odvoji, to potencijalno može izazvati trombotski i/ili embolijski događaj.

#### Mere predostrožnosti

1. Proceduru postavljanja sredstva FemoSeal™ Vascular Closure System treba da urade lekari sa adekvatnom obukom za upotrebu sredstva.
2. Uradite ograničeni femoralni angiogram ili femoralnu punkciju vođenu ultrazvukom pre nego što postavite FemoSeal™ Vascular Closure System.

3. Obustavite proceduru u sledećim slučajevima:
  - Prečnik lumena zajedničke femoralne arterije < 5 mm.
  - Stenoza i/ili znatan plak prisutni u blizini mesta punkcije zajedničke femoralne arterije.
  - Arterijska punkcija je na bifurkaciji femoralne arterije ili distalno u odnosu na nju.
  - Nepravilne grane ili abnormalnosti krvnog suda prisutni u blizini mesta punkcije zajedničke femoralne arterije.
4. Ako postoji hematoma, mora se posebno obratiti pažnja na pravilno uvođenje košuljice konusnog kućišta u arteriju.
5. Primenite tehniku jedne punkcije zida. Ne punktirajte posteriorni zid arterije.
6. Uvek se pridržavajte sterilne tehnike kada koristite FemoSeal™ Vascular Closure System.
7. FemoSeal™ Vascular Closure System je samo za jednokratnu upotrebu i ne treba ga nikako ponovo sterilisati ili koristiti. Jedinica FemoSeal™ je dizajnirana tako da ne može da se koristi ponovo.
8. Ako tokom postavljanja unutrašnje zaptivke naidete na neočekivan otpor, obustavite proceduru.
9. Za pravilno postavljanje unutrašnje zaptivke ponovo postavite palac tako da dugme može slobodno da se vrati i prvobitni položaj.
10. Postarajte se da košuljica konusnog kućišta jedinice FemoSeal™ bude ispod površine kože pre postavljanja spoljašnjeg diska za fiksiranje. Spoljašnji disk za fiksiranje može nenamerno da se postavi iznad nivoa kože kod pacijenata sa malim rastojanjem između femoralne arterije i nivoa kože.
11. Da bi postavljanje bilo pravilno, može biti neophodno da se pre postavljanja na koži napravi rez.
12. Ako je unutrašnja zaptivka je unutar arterije, ali nije moguće potpuno pritisnuti dugme i postaviti spoljašnji disk za fiksiranje, te će hirurg možda morati da ukloni FemoSeal™ elemente za zatvaranje.
13. Ako postane neophodna ponovna punkcija iste femoralne arterije u roku od 18 meseci, ponovna punkcija bi trebalo da se uradi najmanje jedan centimetar proksimalno u odnosu na prethodno mesto pristupa sredstva FemoSeal™ Vascular Closure System.
14. Uputite pacijenta da se pridržava uputstava lekara u vezi sa proverom mesta zatvaranja.

15. Uputite pacijenta da nosi sa sobom Karticu za implantat za pacijenta u narednih 18 meseci

### **Mere predostrožnosti u vreme otpuštanja**

Pre nego što razmotrite otpuštanje, procenite sledeća klinička stanja kod pacijenta:

1. Krvarenje i/ili hematoma na mestu zatvaranja.
2. Bol u toku hodanja.
3. Znaci infekcije na mestu zatvaranja.

### **1.3.3 Bezbednosne korektivne radnje na terenu**

Postojala je jedna bezbednosna korektivna radnja na terenu u vezi sa FemoSeal™ VSC u periodu od 1. septembra 2019. do 31. avgusta 2024. godine.

U 2022. godini, kompanija Terumo dobrovoljno je opozvala FemoSeal™ VCS zbog žalbi koje su se odnosile na neuspehe u testiranju procesa i predstavljanja serije proizvoda FemoSeal za merenje sile potiskivanja i sile retrakcije koju je proizvela kompanija Elkton. Ukupno je povučeno 950 jedinica iz Južne Koreje.

### **1.4 Rezime kliničke evaluacije i kliničkog praćenja nakon plasiranja na tržište**

**Tabela 1.3** sadrži listu pivotalnih studija koje su sprovedene da bi se FemoSeal™ VCS plasirao na tržište, kao i studija sprovedenih nakon plasiranja na tržište i aktivnostima u kliničkom praćenju nakon plasiranja na tržište. Verzija sredstva korišćena u studiji navedena je u tabeli u nastavku. Prva verzija FemoSeal™ VCS (br. 11200) je bila na tržištu do 2006. godine, dok je sledeća verzija (br. C11202) plasirana na tržište 2006. i trenutno se nalazi na tržištu.

**Tabela 1.3 Rezime pivotalnih studija**

| <b>Funkcionalno testiranje na životinjama pre plasiranja na tržište</b>                                                                                                                                                                                                 | <b>Verzija sredstva</b> |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                   |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                   |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                   |
| <b>Prva klinička studija na ljudima</b>                                                                                                                                                                                                                                 |                         |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                   |

| Završene kliničke studije nakon plasiranja na tržište                                                                           |                               |
|---------------------------------------------------------------------------------------------------------------------------------|-------------------------------|
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                      | C11202<br>(trenutno sredstvo) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                               | C11202<br>(trenutno sredstvo) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | C11202<br>(trenutno sredstvo) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)          | C11202<br>(trenutno sredstvo) |
| Planirane/tekuće kliničke studije nakon plasiranja na tržište                                                                   |                               |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                      | C11202<br>(trenutno sredstvo) |
| Aktivnosti kliničkog praćenja nakon plasiranja na tržište                                                                       |                               |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(trenutno sredstvo) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(trenutno sredstvo) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(trenutno sredstvo) |

#### 1.4.1 Rezime podataka pre plasiranja na tržište (ispitivanja na životinjama i klinička istraživanja)

**Tabela 1.4** u nastavku opisuje studije pre plasiranja na tržište, i ispitivanja na životinjama i klinička istraživanja.

**Tabela 1.4 Rezimei studija pre plasiranja na tržište**

| Funkcionalno testiranje na životinjama pre plasiranja na tržište                                                                                                                                                                                 |                                                                          |                                                    |                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|----------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Naziv studije                                                                                                                                                                                                                                    | Godina/CI                                                                | Tip studije                                        | Ciljevi                                                                                                                                                                                                                                        | Faze                                                                                                                                                                                                                                                             | Kriterijumi potencijalne prihvatljivosti                                                                                                                                                                                                                                                                                                                                                                       |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed | 2000<br>Radi Medical System AB<br><br>Sproveo<br>Biomatech,<br>Francuska | Studija na životinjama, eksplorativno istraživanje | Cilj studije je bio da se procene biokompatibilnost i biofunkcionalnost biorazgradivog implantata dizajniranog za postizanje hemostaze u vaskularnom sistemu. Sažetak se bavi rezervnim životinjama iz studije broj 862 (dokument br. 1051-01) | N = 3 odrasle ovce, 1 životinja po vremenskoj tački<br><br>Kontrola radi histopatološke analize, makroskopskog klasifikovanja i ultrastrukturne analize<br><br><ul style="list-style-type: none"> <li>12 meseci</li> <li>15 meseci</li> <li>18 meseci</li> </ul> | Prohodnost arterije <ul style="list-style-type: none"> <li>Procena protoka krvi nakon postavljanja – 2/3 smanjenje protoka krvi povezano sa privremenim arterijskim vazospazmom koji je pripisan proceduri, oba su se desila u levoj zajedničkoj karotidnoj arteriji</li> <li>Procena kolor dopler ultrazvukom (4 nedelje) – 3/3 (100%) bez većeg smanjenja protoka krvi 30 dana nakon implantacije</li> </ul> |

|                        |  |  |  |                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
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| by Biomatech, France). |  |  |  | Kontrola kolor dopler ultrazvukom – 30 dana na pristupnim mestima na karotidnoj i femoralnoj arteriji | <p>Makroskopske opservacije</p> <ul style="list-style-type: none"> <li>• 12 meseci – makroskopski potvrđena prohodnost zbog odsustva anatomske vidljive okluzije; nema makroskopskih lokalnih lezija zbog intolerancije (krvarenje, nekroza ili neovaskularizacija); enkapsulacija unutrašnjeg diska je izražena</li> <li>• 15 meseci – makroskopska opservacija nije pokazala znake inflamacije; nisu identifikovani ostaci unutrašnjeg ili spoljašnjeg diska; enkapsulacija tkivom locirana u oblasti spoljašnjeg diska izgleda isto kao prilikom opservacije u 12. mesecu</li> <li>• 18 meseci – makroskopska opservacija nije pokazala znake lokalne intolerancije, spoljašnji disk vidljiv (3/3 slučajeva), razlaganje unutrašnjeg diska potpuno; 1/3 (leva zajednička karotidna arterija) – uočena depresija zida arterije na mestu implantata (moglo bi da bude povezano sa postavljanjem sredstva)</li> </ul> <p>Zaključci</p> <ul style="list-style-type: none"> <li>• Makroskopski, 12, 15 i 18 meseci nakon implantacije nisu uočeni nekrotični, degenerativni ili trombotski znaci.</li> <li>• Proces razlaganja unutrašnjeg i spoljašnjeg diska se odvijao između 12 i 18 meseci i izgledao je nepotpuno u 18. mesecu, uz beličasto tkivo koje pokrivalo implantiranu oblast.</li> <li>• Histološki, nakon 18 meseci, polimerni materijal više nije bio vidljiv, ali je bilo prisutno endoluminalno fibrozno tkivo. Nisu uočene nekrotične, degenerativne ili trombotske lezije.</li> </ul> |
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| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002 Radi Medical System AB</p> <p>Sproveo Biomatech, Francuska</p> | <p>Studija na životinjama, eksplorativno istraživanje</p> | <p>Cilj studije je bio da se proceni biokompatibilnost biorazgradivog implantata dizajniranog za postizanje hemostaze u vaskularnom sistemu.</p> | <p>Praćenje (nakon implantacije)</p> <ul style="list-style-type: none"> <li>• 12 nedelja</li> <li>• 24 nedelje</li> <li>• 36 nedelja</li> </ul> <p>N = 12 ovaca, 3 životinje po vremenskoj tački, 3 rezervne životinje žrtvovane u 12, 15 i 18 mesecu</p> <p>Mesta implantacije – desna i leva femoralna arterija, desna i leva zajednička karotidna arterija</p> <p>Analiza kolor dopler ultrazvukom</p> | <p><u>Prohodnost karotidne i femoralne arterije nakon 4 nedelje</u></p> <ul style="list-style-type: none"> <li>• Znatno smanjenje protoka krvi 0/12 (0%)</li> </ul> <p><u>Nema znatnog smanjenja protoka krvi</u></p> <ul style="list-style-type: none"> <li>• Ozbiljno narušavanje protoka krvi u vezi sa uvođenjem sredstva 0/12 (0%)</li> <li>• Smanjenje protoka krvi u levoj zajedničkoj karotidi 2/12 (16,6%) zbog privremenog arterijskog vazospazma (pripisano operaciji, ne sredstvu)</li> </ul> <p><u>Narušavanje protoka krvi prema praćenju</u></p> <p>12 nedelja – 0/12 (0%)</p> <p>24 nedelja – 0/12 (0%)</p> <p>36 nedelje – 0/12 (0%)</p> <p>Merenja krvnog pritiska (3 ovce – 36 nedelja)</p> <ul style="list-style-type: none"> <li>• Nije uočeno znatno smanjenje protoka krvi</li> </ul> <p>Makroskopski podaci o integraciji i razlaganju (klasa 0–4)</p> <p><u>Mesta na karotidi</u></p> <p><u>Unutrašnja strana</u></p> <p>-enkapsulacija</p> <p>12 nedelja 1,3</p> <p>24 nedelje 0,8</p> <p>36 nedelja 0,7</p> <p>-razlaganje materijala</p> <p>12 nedelja 2,2</p> <p>24 nedelje 2,3</p> <p>36 nedelja 0,7</p> <p><u>Spoljašnja strana</u></p> <p>-enkapsulacija</p> <p>12 nedelja 2,0</p> <p>24 nedelje 1,0</p> <p>36 nedelja 0,8</p> <p>-razlaganje materijala</p> <p>12 nedelja 2,0</p> |
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|  |  |  |  |  | 24 nedelje 2,7<br>36 nedelja 3,2<br><br><u>Femoralne lokacije</u><br>Spoljašnja strana<br>-enkapsulacija<br>12 nedelja 1,0<br>24 nedelje 2,7<br>36 nedelja 1,0<br>-razlaganje materijala<br>12 nedelja 2,0<br>24 nedelje 2,4<br>36 nedelja 3,0<br><br>Unutrašnja strana<br>-enkapsulacija<br>12 nedelja 2,0<br>24 nedelje 1,2<br>36 nedelja 1,0<br>-razlaganje materijala<br>12 nedelja 1,0<br>24 nedelje 2,2<br>36 nedelja 3,0<br><br><u>Histološki podaci o</u><br><u>integraciji, razlaganju i</u><br><u>inflamatornim parametrima</u><br><u>(srednje relevantne vrednosti,</u><br><u>indeks 0-4) n = 6</u><br><br><u>Mesta na karotidi</u><br>Spoljašnja fibroza<br>12 nedelja – 2,3<br>24 nedelje – 2,3<br>36 nedelja –1,8<br>Unutrašnja neointima<br>12 nedelja – 3,0<br>24 nedelje – 2,7<br>36 nedelja – 3,3<br>Razlaganje materijala<br>12 nedelja – 1,7<br>24 nedelje – 3,0<br>36 nedelja – 3+<br>Inflamatorni parametri<br>(makrofage)<br>12 nedelja – 3,0<br>24 nedelje – 1,7<br>36 nedelja – 1,7<br><u>Femoralne lokacije</u><br>Spoljašnja fibroza<br>12 nedelja – 1,3 |
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|  |  |  |  |  | 24 nedelje – 1,5<br>36 nedelja – 1,7<br>Unutrašnja neointima<br>12 nedelja – 3,7<br>24 nedelje – 3,3<br>36 nedelja – 3,8<br>Razlaganje materijala<br>12 nedelja – 2,0<br>24 nedelje – 3,0<br>36 nedelja – 3+<br>Inflamatorni parametri<br>(makrofage)<br>12 nedelja – 3,5<br>24 nedelje – 1,8<br>36 nedelja – 1,8<br><br><u>Histomorfološke vrednosti</u><br><u>prohodnosti</u><br>Mesta na karotidi<br>12 nedelja 74,0%<br>24 nedelje 81,9%<br>36 nedelja 89,43%<br>Femoralna mesta<br>12 nedelja – 42,2%<br>24 nedelje – 73,21%<br>36 nedelja – 78,71%<br><br><u>US prohodnost krvnog suda</u><br><u>(srednja vrednost %)</u><br>Mesto na karotidi<br>12 nedelja 94,6%<br>24 nedelje – 96,7%<br>36 nedelja – 94,7%<br>Femoralna mesta<br>12 nedelja – 66,9%<br>24 nedelje – 63,6%<br>36 nedelja – 75,1%<br><br>Zaključci <ul style="list-style-type: none"> <li>Nije uočen značajan znak lokalne intolerancije (odsustvo vidljivih inflamatornih, nekrotičnih ili degenerativnih lezija) u 12, 24. ili 36. nedelji</li> <li>Nisu zabeležene značajne neželjene tkivne reakcije u smislu matičnog tkiva i sredstva</li> <li>Razlaganje implantata je bilo gotovo završeno u 36. nedelji</li> </ul> |
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| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France). | 2002. Radi Medical System AB Sproveo Biomatech, Francuska | Studija na životinjama | Svrha studije je bila procena biokompatibilnosti i biofunktionalnosti biorazgradivog materijala dizajniranog za postizanje hemostaze u vaskularnom sistemu. Predviđeno je da ispitano sredstvo uđe u otvor punkcije u arterijama da bi se postigla hemostaza. Jedan disk je ušao u otvor punkcije u arteriji, a drugi je zategao unutrašnji disk sa spoljašnje strane arterije. Oba diska su umetnuta kroz košuljicu uvodnika. Diskovi su dizajnirani da spreče krvarenje, zarastu u zid krvnog suda i da se na kraju razlože i resorbuju. Studija je dizajnirana za sakupljanje i analiziranje podataka nakon funkcionalne implantacije kod ovaca i svinje radi procene kapaciteta implantata da održi fiziološku funkciju kada se koristi u cirkulatornom sistemu, da bi se utvrdili reagovanje domaćina i reagovanje sredstva (fizički integritet, tkivna enkapsulacija u žrtvovanju) i da bi se procenilo razlaganje implantata | Period implantacije / praćenje je 5 nedelja za sve životinje<br><br>4 ovce, 1 svinja<br><br>14 elemenata za zatvaranje<br><br>8 elemenata za zatvaranje implantiranih u 2 ovce,<br><br>2 elementa za zatvaranje implantirana u 1 svinju<br><br>Kada su dva elementa za zatvaranje implantirana u istu femoralnu arteriju, implantirani su na rastojanju od > 30 mm | Nisu zabeleženi kriterijumi za neželjene znake (inflamacija, nekroza, krvarenje ili bilo koja druga lezija) ni bilo kakvo formiranje tankog pseudointimalnog sloja. Naročita pažnja je posvećena početnoj tkivnoj integraciji sredstva, uz poseban akcenat za enkapsulaciju unutrašnjeg diska.<br><br>Makroskopski, nisu uočeni značajni znaci lokalne intolerancije ili formiranja tromba. Makroskopska opservacija nije otkrila razliku između ovce i svinje nakon implantacije elemenata za zatvaranje u femoralnim arterijama. Makroskopski, nisu uočeni značajni znaci lokalne intolerancije ili formiranja tromba. Makroskopska opservacija nije otkrila razliku između ovce i svinje nakon implantacije elemenata za zatvaranje u femoralnim arterijama.<br><br>Histopatološka analiza mesta implantacije kod ovce nije pokazala lokalne neželjene reakcije. Unutrašnji i spoljašnji disk su pokazali znake razlaganja i u nekim slučajevima su bili polomljeni na sitnije delove. Unutrašnji diskovi su potpuno integrisani u neointimalno tkivo. Kod svinje je histopatološka analiza pokazala nešto više inflamatornih znakova oko unutrašnjeg i spoljašnjeg diska. Kod obe životinje |
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|                                                                                                                                                                                                              |                               |                                                       |                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                    | <p>multifilament je pokazao nešto više inflamatornih znakova nego materijal diska, što je normalno kod upletenih hirurških konaca zbog veće površine.</p> <p>Prohodnost krvnog suda je merena nakon 5 nedelja primenom tri različite metode, histomorfometrije, histomorfometrije u kombinaciji sa merenjem prečnika krvnog suda upotrebom kljunastog merila i upotrebom kolor dopler ultrasonografijom. Srednja vrednost prohodnosti krvnog suda kod ovce je bila između 60% i 80% u zavisnosti od metoda (12 opservacija). Kod svinje je srednja vrednost prohodnosti krvnog suda bila između 40% i 80% (2 opservacije).</p> |
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| <b>Prva klinička studija na ljudima</b>                                                                                                                                                                      |                               |                                                       |                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>Naziv studije</b>                                                                                                                                                                                         | <b>Godina/CI</b>              | <b>Tip studije</b>                                    | <b>Ciljevi</b>                                                                                                                                                                                                                                                                                                                         | <b>Faze</b>                                                                                                                                                                                                                                                                                                                                                                        | <b>Kriterijumi potencijalne prihvatljivosti</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004. Radi Medical Systems AB | Otvoreno, multicentrično ispitivanje sa jednom grupom | Ciljevi studije su bili utvrđivanje bezbednosti, performansi i delotvornosti sredstva FemoSeal Vascular Closure System (FemoSeal sistem) u načelu, a naročito elemenata za zatvaranje, kod pacijenata koji se podvrgavaju kardiološkim dijagnostičkim ili interventnim kardiološkim procedurama sa pristupom preko femoralne arterije. | <p>Studija iz 2 dela</p> <p>Ukupno n = 80</p> <p>Deo 1 n = 20</p> <p>Deo 2 n = 60</p> <p>Indikacije:</p> <p>Deo 1 – dijagnostička kateterizacija srca sa femoralnom arterijom kao mestom pristupa</p> <p>Deo 2 – pacijenti koji se podvrgavaju dijagnostici i interventnim kardiološkim procedurama sa pristupom preko femoralne arterije</p> <p>Praćenje u periodu od 30 dana</p> | <p>Ishodi</p> <p><u>-hemostaza je postignuta sa FS-om bez kompresije</u></p> <p>- Deo 1 20/20 (100%)</p> <p>- Deo 2 58/60 (97%)</p> <p>Srednje vreme do hemostaze u vreme procedure (deo 2) – 1,0 minut (opseg za direktno – 8 minuta)</p> <p><u>Vreme do ambulacije (u minutima)</u></p> <p>Deo 1 – Srednje: 33,0</p> <p>srednja vrednost: 67,8</p> <p>Deo 2 –</p>                                                                                                                                                                                                                                                            |

|  |  |  |  |  | srednja vrednost: 45<br>srednja vrednost: 87,5<br><br><u>Incidenca ozbiljnih vaskularnih komplikacija – praćenje u periodu od 30 dana</u><br>Deo 1<br>-Bez vaskularnih komplikacija 20/20 (100%)<br>Deo 2<br>Pseudoaneurizma – 1/59 (1,69%)<br><br><u>Neuspešno lečenje</u><br>Deo 1 – 0/20 (0%)<br>Deo 2 – 3/60 (5%) <ul style="list-style-type: none"> <li>2 zbog neuspešnog postizanja hemostaze bez primene kompresije</li> <li>1 zbog ozbiljne vaskularne komplikacije, pseudoaneurizme</li> </ul> <u>Uporno curenje</u><br>Deo 1 – 0/20 (0%)<br>Deo 2 – 8/60 (13%)<br><br><u>Hematom</u><br>Deo 1 – 0/20 (0%)<br>Deo 2 – 6/60 (10%) |
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U okviru plana razvoja pre plasiranja na tržište sredstva FemoSeal™ VCS urađena su 3 funkcionalna ispitivanja na životinjama. U 2000. pre pokretanja kliničkih studija urađena je studija na životinjama radi procene biofunkcionalnosti sredstva FemoSeal™ VCS. Ova studija je procenjivala kapacitet elemenata za zatvaranje da održe fiziološku funkciju i njihovo razlaganje. U 18. mesecu unutrašnji i spoljašnji disk više nisu bili vidljivi, a zamenilo ih je endoluminalno fibrozno tkivo. U zaključku je potvrđen kapacitet FemoSeal™ VCS elementa za zatvaranje da održi fiziološku funkciju kada se koristi u cirkulatornom sistemu.

U 2002. godini je urađena studija na životinjama da bi se procenile biokompatibilnost i biofunktionalnost biorazgradivog implantata, FemoSeal™ VCS, dizajniranog za postizanje hemostaze u vaskularnom sistemu. U sažetku, razlaganje implantata je bilo gotovo okončano do 36. nedelje i nije bilo značajnih neželjenih tkivnih reakcija.

Još jedna studija na životinjama iz 2002. godine procenjivala je biokompatibilnost i biofunktionalnost biorazgradivog implantata, FemoSeal™ VCS, dizajniranog za postizanje hemostaze u vaskularnom sistemu. Nakon 5 nedelja enkapsulacija diska je bila potpuna, a znaci razlaganja su uočeni na unutrašnjem i spoljašnjem disku. U zaključku je potvrđen kapacitet implantata da održi fiziološku funkciju kada se koristi u cirkulatornom sistemu.

U okviru plana kliničkog razvoja sredstva FemoSeal™ VCS, Radi Medical System AB je sproveo kliničko istraživanje pre plasiranja na tržište. Ovo kliničko istraživanje nije objavljeno i nije dostupno na internetu. Studija modela sredstva br. 11200 je sprovedena u periodu 2002–2004. prema evropskom standardu EN 540 (Kliničko istraživanje medicinskih sredstava za ljudske ispitanike) i u skladu sa IHC Opštim pitanjima u vezi sa kliničkim ispitivanjima i Smernicama za dobru kliničku praksu. Detaljni podaci iz ove studije su dokumentovani u sažetku EU-SE-001. Kliničko ispitivanje je dokumentovano u Završnom sažetku Radi Medical Systems AB, „Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures“. Klinička studija je sprovedena sa prvim FemoSeal™ modelom br. 11200 i fokusirala se na bezbednost i delotvornost implantabilnih komponenata za zatvaranje. Jedina razlika između prvog modela br. 11200 i aktuelnog modela, C11202 su frenč veličina, 6 F odnosno 7 F, i unapređen sistem dovoda. Kliničke koristi, namena, principi rada i sirovi materijali implantabilnih sistema za zatvaranje, unutrašnji i spoljašnji disk za fiksiranje su nepromenjeni.

Sredstvo je bilo namenjeno pacijentima koji se podvrgavaju dijagnostičkim kardiološkim i interventnim kardiološkim procedurama sa mestom pristupa preko femoralne arterije. Cilj ove studije bio je da se utvrde bezbednost, performanse i delotvornost sredstva FemoSeal™ VCS. Ovo je bila prospektivna, multicentrična otvorena studija sa jednom grupom i praćenjem u periodu od 30 dana.

Primarni parametar praćenja za performanse je bilo vreme do postizanja hemostaze definisano kao odsustvo jakog krvarenja. Primarni bezbednosni parametar praćenja bio je incidenca ozbiljnih vaskularnih komplikacija u periodu od 30 dana. Sekundarni parametri praćenja obuhvatali su ambulaciju, proporciju neuspešnih lečenja, incidencu neželjenih događaja i karakteristike performansi sredstva tokom dovoda i postavljanja.

Pacijenti obuhvaćeni ovom studijom bili su odrasle osobe koje su mogle da daju informisani pristanak i imaju najmanje jedan očuvani puls na stopalu. Pacijenti su isključivani iz studije ako su imali neko od sledećih stanja:

- Istorija oboljenja perifernih krvnih sudova

- Autoimuna bolest
- Poznat poremećaj krvarenja ili ozbiljna anemija
- INR > 1,5
- Infarkt miokarda u protekla 72 sata
- Nekontrolisana hipertenzija uprkos terapiji
- Gojaznost koja sprečava pristup Seldingerovom tehnikom
- Postojanje vaskularnog grafta ili stenta na mestu arteriotomije
- Ranija ipsilateralna punkcija u periodu od 3 meseca
- Očekivani životni vek < 6 meseci

Osim toga, pacijenti su pregledani intraoperativno i isključivani iz studije ako je uočeno bilo šta od navedenog:

- Prečnik lumena zajedničke femoralne arterije < 5 mm
- Grane arterije 2 cm proksimalno u odnosu na mesto punkcije
- Značajna stenoza u oblasti od 3 cm od mesta punkcije
- Upotreba primarne košuljice uvodnika > 6 Fr
- Punkcija na račvanju femoralne arterije ili distalno u odnosu na njega
- Više femoralnih punkcija
- Poznata ili suspektna punkcija posteriornog zida femoralne arterije
- Veliki hematoma (2:6 cm) po završetku procedure
- Otežano umetanje primarne košuljice za proceduru zbog krivudavog tkiva ili krvnog suda

Ova studija sa jednim protokolom je sprovedena iz dva dela: 20 pacijenata je uključeno u toku Dela 1, zatim je urađena analiza bezbednosti, pa je uključeno još 60 pacijenata u toku Dela 2.

U Delu 1 srednja starosna dob uključenih pacijenata je bila 65,9 godina, 70,0% pacijenata je bilo muškog pola, a 95% pacijenta je istovremeno uzimalo druge lekove. U Delu 2 studije srednja starosna dob je bila 63,8 godina, 78% pacijenata je bilo muškog pola, a 100% njih je istovremeno uzimalo druge lekove.

U studiju su mogli da se uključe pacijenti koji su podvrgnuti dijagnostičkim (Deo 1 i Deo 2) ili interventnim (Deo 2) procedurama kateterizacije srca. Procedure su bile usaglašene sa standardom nege u svakoj od bolnica koje su učestvovala u uključivanju, nakon čega je sledila

primena sredstva FemoSeal™ VCS. Podaci o pacijentima su sakupljeni prilikom početne posete, u toku procedure i 1. i 30. dana nakon procedure. Rezultati su rezimirani u **tabeli 1.5** i pokazuju da je sredstvo FemoSeal™ VCS bezbedno i delotvorno za primenu u ovoj populaciji pacijenata.

**Tabela 1.5 Klinički rezultati prijavljeni u studiji pre plasiranja na tržište**

|                                                                                                     | Deo 1       | Deo 2                    |
|-----------------------------------------------------------------------------------------------------|-------------|--------------------------|
| Broj pacijenata                                                                                     | 20          | 60                       |
| Srednje vreme do hemostaze                                                                          | 1,2 minuta  | 1,6 minuta <sup>a</sup>  |
| Srednje vreme do ambulacije                                                                         | 72,2 minuta | 87,5 minuta <sup>b</sup> |
| Incidenca ozbiljnih vaskularnih komplikacija <sup>c</sup>                                           | 0 (0%)      | 1 (2%)                   |
| Broj pacijenata sa neželjenim događajima                                                            | 5 (25%)     | 19 (32%)                 |
| Neuspešno lečenje (definiše se ka ozbiljna vaskularna komplikacija, potreba za kompresijom ili oba) | 0 (0%)      | 3 (5%)                   |
| Otkazivanja sredstva                                                                                | 0 (0%)      | 6 (10%)                  |

<sup>a</sup>Na osnovu ukupnog uzorka od 58 jer kod 2 pacijenta nije postignuta hemostaza u vreme procedure zbog prethodnih ipsilateralnih punkcija. Hemostaza je kod ovih pacijenata postignuta u 7. i 37. minutu.

<sup>b</sup>Na osnovu ukupnog uzorka od 59: 1 pacijent nije bio uključen jer je stavljen na ventilator zbog plućnog edema i nemogućnosti ambulacije duže od jedne nedelje.

<sup>c</sup>Definisano kao vaskularna komplikacija koja zahteva transfuziju krvi ili hiruršku reparaciju ili lokalna infekcija koja zahteva administraciju antibiotika, hospitalizaciju ili produženu hospitalizaciju ili debridman mesta

U Delu 1 studije nisu uočene ozbiljne vaskularne komplikacije. Prijavljena je 1 ozbiljna vaskularna komplikacija u Delu 2 studije: pseudoaneurizma koja je prijavljena u periodu od 1 dana nakon procedure. Događaj je zahtevao kompresiju vođenu ultrazvukom i injekciju trombina u pseudoaneurizmu i produžetak hospitalizacije pacijenta.

Od 5 neželjenih dejstava prijavljenih u Delu 1 studije, moguće je da je 1 neželjeni događaj bio povezan sa sredstvom: događaj koji se ne smatra ozbiljnim, jako krvarenje 1 dan nakon procedure. Od 19 neželjenih događaja prijavljenih u Delu 2 studije, uočena su 3 neželjena događaja u vezi sa sredstvom koji se ne smatraju ozbiljnim i 6 događaja koji su moguće povezani sa sredstvom i koji se ne smatraju ozbiljnim, uključujući 3 izveštaja o upornom curenju, 2 hematoma i 1 slučaj bola u nozi nakon vežbanja.



Kod 3 pacijenta u Delu 2 smatralo se da je lečenje neuspešno: 2 usled nepostizanja hemostaze bez korišćenja kompresije i 1 usled ozbiljne vaskularne komplikacije (pseudoaneurizme).

U Delu 1 studije nije bilo neuspešnih lečenja.

Od šest otkazivanja sredstva u Delu 2 studije, tri nisu ometala proceduru, jedno je pripisano grešci korisnika, jedno se odnosilo na curenje uvodnika i jedno je bilo prekinut spoj filameta. Poslednja dva problema su rešena unapređenjem modela koje je implementirano u C11202.

Deo 2 kliničke studije pre plasiranja na tržište nije prijavio rezultate praćenja u periodu od 6 meseci zbog neusaglašenosti pacijenata. Rezultati kliničke studije pre plasiranja na tržište (EU-SE-001) za period od 30 dana, koja je u skladu sa periodom praćenja u kliničkoj literaturi, pokazuju da je sredstvo FemoSeal™ VCS bezbedno i delotvorno.

#### 1.4.2 Sažetak podataka iz kliničkih ispitivanja nakon plasiranja na tržište

Postoje 4 završene kliničke studije nakon plasiranja za tržište koje su opisane u tabeli 1.6 u nastavku. Ova klinička istraživanja nisu objavljena i nisu dostupna na internetu.

**Tabela 1.6 Kliničke studije nakon plasiranja na tržište**

| Završene kliničke studije nakon plasiranja na tržište                                       |                                    |                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                              |
|---------------------------------------------------------------------------------------------|------------------------------------|--------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Naziv studije                                                                               | Godina/CI                          | Tip studije                                                                          | Ciljevi                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | Faze                                                                                                                                                                                                                                                                                                                                              | Kriterijumi potencijalne prihvatljivosti                                                                                                                     |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006. RADI                         | Studija nakon plasiranja na tržište, prihvatanje novog pakovanja od strane korisnika | Studija nakon plasiranja na tržište sprovedena je na ažuriranom modelu FemoSeal Vascular® sistema za zatvaranje vaskularnog pristupa br. 11202 koje sadrži modifikovani sistem za dovod u poređenju sa prvim modelom, br. 11200, da bi se dokumentovala funkcionalnost.<br><br>Cilj studije je bio da se dobiju povratne informacije o revidiranom Uputstvu za upotrebu, projektu za obuku lekara i medicinskih sredstava, da se potvrde ocene iz analize rizika i da bi se dobile informacije za unapređenja kvaliteta proizvoda. | 100 pacijenata <ul style="list-style-type: none"> <li>63 muškarca / 37 žene</li> <li>Srednja starosna dob 68 godina za žene, 65 godina za muškarce</li> </ul> 2 švedske bolnice, 6 lekara<br><br>112 sredstava<br><br>Podaci sakupljeni iz obrazaca evidencije pacijenata (CRF)<br><br>Planirano vreme opservacije – 30 minuta od vremena primene | Ishodi<br><br>1. Ilustracije/uputstva u Uputstvu za upotrebu smatraju se informativnim i adekvatnim<br><br>2. Neposredna hemostaza (91/100)                  |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)           | Dr. Nicolas Moes Innsbruck Medical | Potvrдна ocena nakon plasiranja na tržište                                           | Cilj ove studije bio je da se ocene bezbednost i performanse sredstva FemoSeal® koje se koristi u toku normalne kliničke rutine                                                                                                                                                                                                                                                                                                                                                                                                    | 50 uzastopnih pacijenata<br><br>Indikacija – dijagnostička ili invazivna kateterizacija srca                                                                                                                                                                                                                                                      | Primarni parametri praćenja <ul style="list-style-type: none"> <li>Primarni parametar praćenja efikasnosti – TTH (vreme do hemostaze) sa curenjem</li> </ul> |

|                                                                                |                     |                                     |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|--------------------------------------------------------------------------------|---------------------|-------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|-----|----------|-------|----------|-----------|----|-----------|-----------|-------------------------|----------|--------------------|------------|---------------------|-----------|-------------------|---------|-----------------------|----------|--------------------------------|----------|----------------------|-----------|--------------------------|-----------|-----------------------------------|----------|----------------------|--------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                | University, Austria |                                     | <p>kod pacijenata koji se podvrgavaju dijagnostičkoj kateterizaciji srca ili perkutanoj kardiološkoj interventnoj proceduri koja se radi sa košuljicom od 7 F.</p>                                                                                                                                                                    | <p>preko zajedničke femoralne arterije</p> <table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                                                                                                                                                                                                                                                                                                    | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | <p>ili bez njega, ali bez dodatne kompresije, ručne ili mehaničke.</p> <ul style="list-style-type: none"><li>Bezbednosni parametar praćenja – incidenca neželjenih događaja – manje i ozbiljne vaskularne komplikacije i svi drugi neželjeni događaji – ozbiljni i oni koji se ne smatraju ozbiljnim u toku trajanja studije (tj. do otpuštanja pacijenta).</li></ul> <p>Ishodi</p> <ul style="list-style-type: none"><li>Srednje vreme do hemostaze</li><li>Dijagnostika – 56,6 ± 29 sekundi</li><li>Intervencija 59,9 ± 16,2 sekundi</li><li>Svi pacijenti 57,8 ± 26,3</li><li>Svi pacijenti su mogli da se ambuliraju nakon 4 sata ležanja bez ikakvih problema.</li></ul> <p>Bezbednosni ishodi</p> <ul style="list-style-type: none"><li>49/50 (98%) bez vaskularnih komplikacija do otpuštanja iz bolnice</li><li>Srednje vreme do otpuštanja 2,6 dana</li><li>1/50 (2%) manje krvarenje sledećeg dana nakon ambulacije bez događaja na dan angiografije</li></ul> |
| n                                                                              | 50                  |                                     |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| men                                                                            | 35 (70%)            |                                     |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| women                                                                          | 15 (30%)            |                                     |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| PCI cases                                                                      | 15                  |                                     |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| age (yrs)                                                                      | 62.8±11.1           |                                     |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| body mass index (kg/m²)                                                        | 25.4±6.7            |                                     |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| systolic BP (mmHg)                                                             | 131.2±20.9          |                                     |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| diastolic BP (mmHg)                                                            | 77.9±10.6           |                                     |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| diabetes mellitus                                                              | 9 (18%)             |                                     |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| arterial hypertension                                                          | 34 (68%)            |                                     |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| previous coronary intervention                                                 | 13 (26%)            |                                     |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| preprocedure aspirin                                                           | 50 (100%)           |                                     |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| preprocedure clopidogrel                                                       | 50 (100%)           |                                     |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Procedural unfractionated heparin                                              | 15 (30%)            |                                     |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Procedural abciximab                                                           | 2 (4%)              |                                     |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009) | 2009 RADI           | Studija nakon plasiranja na tržište | <p>Studija bi trebalo da informiše o tome da li su kupci/korisnici uočili neke probleme sa novim pakovanjem, naročito sa nesterilnim spoljašnjim delom Tuvek/PET-PE vrećice.</p> <p>Studija bi takođe trebalo da pruži informacije o tome da li lekar uočava neke razlike u koracima primene/postavljanja sredstva u poređenju sa</p> | <p>25 sredstava</p> <p>4 švedske bolnice</p> <p>16/25 (64%) pacijenata su bili PCI pacijenti sa jakom dozom antikoagulantnih lekova</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | <p>Ishodi</p> <ol style="list-style-type: none"><li>Problemi u vezi sa pakovanjem – 21/25 (84%) primena je bilo uspešno; 4/25 (16%) je bilo neuspešno (1 – testiranje novog uvodnika, 1 unutrašnji disk je prošao kroz arteriotomiju u koraku povlačenja, dugme je izašlo i spoljašnji disk je plasiran u kanal reza na tkivu, 2 neposredna hemostaza nije postignuta uprkos problemima sa postavljanjem.)</li></ol> |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |

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|---------------------------------------------------------------------------------------------------------------------------------|---------------------------------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                 |                                 |                                                                                | sredstvima koje je ranije koristio.                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 2. Pacijenti sa neposrednom hemostazom 19/25 (76%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|                                                                                                                                 |                                 |                                                                                | Studija bi trebalo i da pruži informacije o budućoj potrebi za unapređenje kvaliteta proizvoda.                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 3. Krvarenje 11/25 (44%) – 9/25 (36%)<br>curenje/krvarenje, 2/25 (8%) hematomi<br>Ukupna stopa događaja 19%                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022) | 2022/Terumo Medical Corporation | Prospektivna, multicentrična, opservaciona studija nakon plasiranja na tržište | Da se dalje pokažu bezbednost i delotvornost sredstva FemoSeal™ VCS u postizanju hemostaze mesta pristupa na zajedničkoj femoralnoj arteriji (CFA, engl. common femoral artery) kod stvarnih ispitanika koji se podvrgavaju perkutanim endovaskularnim procedurama | <ul style="list-style-type: none"> <li>Praćenje pacijenta nakon 30 dana (<math>\pm 7</math> dana) posetom bolnici ili telefonskim pozivom.</li> <li>Uključivanje: od decembra 2021. do jula 2022.</li> <li>230 uključenih ispitanika koji se podvrgavaju dijagnostičkim ili interventnim endovaskularnim procedurama u kojima se koristi FemoSeal™.</li> </ul> <p>3 evropske lokacije: Francuska (92 pacijenta), Nemačka (38 pacijenata), Belgija (100 pacijenata).</p> | <ul style="list-style-type: none"> <li><b>Demografski podaci / komorbiditeti:</b> <ul style="list-style-type: none"> <li>- Pol: 161 muškarac (70%) / 69 žena 69 (30%).</li> <li>- Prosečna starost: <math>70 \pm 12</math>.</li> <li>- BMI: <math>26,1 \pm 4,95</math> kg/m<sup>2</sup>.</li> <li>- Hipertenzija: 160 pacijenata (69,6 %).</li> <li>- Dislipidemija: 128 (55,7%).</li> <li>- Oboljenje koronarne arterije: 42 (18,3%).</li> <li>- Aktivni pušač: 86 (37,6%).</li> <li>- Bivši pušač: 66 (28,8%).</li> <li>- Oboljenje koronarne arterije: 34 (14%).</li> <li>- Istorija infarkta miokarda: 18 (7,8%).</li> <li>- Revaskularizacija periferne arterije: 12 (5,2%) karotidne arterije i 83 (37,5%) i arterije donjih ekstremiteta.</li> <li>- Antiagregaciona terapija (na početku): 211 (91,7%), uključujući 21 (9,1%) dualnu antiagregacionu terapiju (DAPT).</li> <li>- Oralna antikoagulacija: 40 (17,4%) pacijenata.</li> </ul> </li> <li><b>Karakteristike intervencije:</b> <ul style="list-style-type: none"> <li>- Okruženje: bolnička klinika 162 slučaja (70,4%), ambulantna klinika 68 slučajeva (29,6%).</li> <li>- Preovlađujuća indikacija: klaudikacija 147 slučajeva (63,9%).</li> </ul> </li> </ul> |

|  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
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|  |  |  |  |  | <p>- Pristup: 35 antegradno (15,3%), 194 retrogradno (84,7%).</p> <p>• <b>Primarni parametri praćenja:</b></p> <p>- Parametar praćenja kombinovane bezbednosti (bez značajnih komplikacija na mestu pristupa u roku od 6 sati nakon postupka) i delotvornosti (uspešna hemostaza na mestu punkcije) postignut je u 215/226 (95,1%) [95% CI: 91,46; 97,55] pacijenata u celoj grupi za analizu i 215/230 (93,5%) [95% CI 89,47, 96,30] u grupi lečenoj sa FemoSeal™.</p> <p>- Parametar praćenja efikasnosti postignut je kod 219/226 (96,9%) CI [93,7, 98,7] pacijenata.</p> <p>- Parametar praćenja bezbednosti postignut je kod 220/230 (95,2%) [95% CI: 92,15, 97,90] pacijenata.</p> <p>• <b>Sekundarni parametri praćenja:</b></p> <p>- Odsustvo manjih komplikacija na mestu pristupa šest sati nakon postupka postignuto je kod 225/230 (97,8%) [95% DI: 95,00; 99,29].</p> <p>- Odsustvo velikih i manjih komplikacija na mestu pristupa od šest sati do 30 dana nakon postupka postignuto je kod 219/230 (95,2%) [95% CI:91,60; 97,59] pacijenata.</p> <p>- Srednje vreme do hemostaze sa FemoSeal™ VCD: 0,42 (0,25; 0,50) minuta.</p> |
|--|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

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|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <ul style="list-style-type: none"> <li>- Srednje vreme do ambulacije 5,00 (4,54; 5,50) minuta.</li> <li>- Srednja dužina boravka u bolnici: 23,98 (22,72, 25,00) sati.</li> <li>- Upotrebljivost sistema FemoSeal™ VCS: „lako“ ili „vrlo lako“ postavljanje u 98,7% slučajeva („lako“ postavljanje u 21 (9,2%), „vrlo lako“ postavljanje u 205 (89,5%)) bez otpora ili sa malim otporom pri postavljanju u 226 (98,3%) slučajeva.</li> </ul> <p>152/230 (66,1%) pacijenata lečenih žicom vodičem uključenom u komplet FemoSeal™ (GW 0,038") i preporučenom u kompletu FemoSeal™ bez prijavljenih nedostataka sredstva ili neželjenih događaja.</p> |
|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Studija iz 2006. godine je sprovedena da bi se potvrdili bezbednost i delotvornost aktuelnog sredstva sa unapređenim sistemom za dovod i za prikupljanje povratnih informacija o Uputstvu za upotrebu sredstva FemoSeal™ VCS i programu obuke. Studija je obuhvatila 100 pacijenata i primarni parametar praćenja je bilo da li je hemostaza postignuta ili su bili potrebni dodatna ručna ili mehanička kompresija. Zaključak ove studije je da je primena sredstva FemoSeal™ VCS bila uspešna u većini slučajeva (91% je postiglo neposrednu hemostazu).

U studiji iz 2008. je učestvovalo 50 pacijenata radi ocene bezbednosti i performansi sredstva FemoSeal™ VCS kada se koristi u uobičajenim kliničkim postupcima kod pacijenata koji se podvrgavaju kateterizaciji srca sa košuljicom od 7 Fr. Primarni parametar praćenja za studiju bio je sakupljanje podataka o vremenu do postizanja hemostaze i vremenu do ambulacije bez dodatne kompresije, ručne ili mehaničke. Rezultati studije su pokazali da je srednje vreme do postizanja hemostaze bilo 57,8 sekundi i da su svi pacijenti ambulirani nakon 4 sata ležanja.

Studija iz 2009. godine je trebalo da proceni novo pakovanje sredstva FemoSeal™ VCS. U studiji je učestvovalo 25 pacijenata. Primarni parametar praćenja bilo je utvrđivanje da li su korisnici imali bilo kakvih problema sa pakovanjem. Korisnici su zabeležili probleme u vezi sa pakovanjem sredstva FemoSeal™ VCS. U ovoj studiji su takođe sakupljeni podaci o vremenu do postizanja hemostaze.

Cilj studije iz 2022. je bio da proaktivno sakupi podaci o bezbednosti i delotvornosti sredstva FemoSeal VCS u postizanju hemostaze mesta pristupa na zajedničkoj femoralnoj arteriji (CFA, engl. common femoral artery) kod stvarnih ispitanika koji se podvrgavaju perkutanim endovaskularnim procedurama. U studiji je učestvovalo 230 pacijenata. Primarni parametri praćenja za registar i uspeh procedure (tj. uspešnu hemostazu mesta punkcije) i smanjenje broja ozbiljnih komplikacija (npr. vaskularne povrede, krvarenje na mestu pristupa, infekcija na mestu pristupa, ponovljena ručna kompresija i ipsilateralna akutna ishemija noge u vezi sa novim mestom pristupa). Studija je zaključila da sredstvo FemoSeal™ VCS dobro funkcioniše u realnim uslovima i pruža efikasnu hemostazu i mali broj komplikacija na mestu pristupa za pacijente koji se podvrgavaju perifernim endovaskularnim intervencijama. Pokazuje dobre performanse sa kratkim vremenom do hemostaze i dobrim povratnim informacijama o dobroj upotrebljivosti za rukovaoca, što FemoSeal™ VCS čini vrednim sredstvom za zatvaranje femoralnog pristupa.

### 1.4.3 Sažetak podataka iz kliničkih praćenja nakon plasiranja na tržište

#### 1.4.3.1 Završeno kliničko praćenje nakon plasiranja na tržište

Sažetak završenih aktivnosti kliničkog praćenja nakon plasiranja na tržište je opisan u **tabeli 1.7** u nastavku.

**Tabela 1.7. Aktivnosti kliničkog praćenja nakon plasiranja na tržište**

| Završene aktivnosti kliničkog praćenja nakon plasiranja na tržište        |           |                                                                        |                                                                                                                                                                                                      |                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|---------------------------------------------------------------------------|-----------|------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Naziv aktivnosti                                                          | Godina/CI | Tip studije                                                            | Ciljevi                                                                                                                                                                                              | Faze                                                                                                                                                     | Kriterijumi potencijalne prihvatljivosti                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021. TMC | Klinička anketa nakon plasiranja na tržište – anketa visokog kvaliteta | Anketa nakon puštanja na tržište za prikupljanje potencijalnih povratnih informacija u vezi sa upotrebom sredstva FemoSeal™ Vascular Closure Device koji se distribuira na tržištima Evropske unije. | <ul style="list-style-type: none"> <li>120 slučajeva</li> <li>8 individualnih lekara sa &gt; 5 godina iskustva</li> <li>Više zemalja u Evropi</li> </ul> | <p><b>Procene sredstva na skali 1–5 – Iskazi iz anketa</b></p> <ul style="list-style-type: none"> <li>Kriterijumi za prihvatanje <ul style="list-style-type: none"> <li>Ocene 3–5 se smatraju povoljnim</li> <li>Svi iskazi bi trebalo da imaju ≥ 80% pozitivnih povratnih informacija</li> </ul> </li> <li>Ishodi <ul style="list-style-type: none"> <li>Nijedan iskaz iz ankete nije dobio &gt; 20% nepovoljnih odgovora</li> <li>Nije podneta nijedna žalba na proizvod</li> </ul> </li> </ul> |

| Završene aktivnosti kliničkog praćenja nakon plasiranja na tržište                                                              |                   |                                                                        |                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|---------------------------------------------------------------------------------------------------------------------------------|-------------------|------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 20210298 – 0.035" and 0038" Guidewire Clinical Survey Report (2021)                                                             | 2021. TMC         | Klinička anketa nakon plasiranja na tržište – anketa visokog kvaliteta | Anketa nakon plasiranja na tržište za prikupljanje potencijalnih povratnih informacija u vezi sa upotrebom žice vodiča od 0,035" koja se koristi sa 6Fr Angio-Seal™ VIP Vascular Closure Device (VCD) i 0,038" koja se koristi sa 8Fr Angio-Seal™ VIP VCD i FemoSeal Vascular Closure System koji se distribuiraju na tržištu Evropske unije. | <ul style="list-style-type: none"> <li>Ankete za žicu od 0,035" <ul style="list-style-type: none"> <li>106 anketa</li> <li>64 lekara</li> </ul> </li> <li>Ankete za žicu od 0,038" <ul style="list-style-type: none"> <li>109 anketa</li> <li>55 lekara</li> </ul> </li> <li>12 retrospektivnih anketa</li> </ul> | <b>Procene sredstva na skali 1–5 – Iskazi iz anketa</b> <ul style="list-style-type: none"> <li>Kriterijumi za prihvatanje <ul style="list-style-type: none"> <li>Ocene 3–5 se smatraju povoljnim</li> <li>Svi iskazi bi trebalo da imaju <math>\geq 80\%</math> pozitivnih povratnih informacija</li> </ul> </li> <li>Ishodi <ul style="list-style-type: none"> <li>Sve žice vodiči su dobile prihvatljive ocene</li> <li>Nije podneta nijedna žalba na proizvod</li> </ul> </li> </ul>                                                                                                                                      |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023–2024. TMC/TE | Klinička anketa nakon plasiranja na tržište – anketa visokog kvaliteta | Da bismo prospektivno prikupili povratne informacije u vezi sa korišćenjem FemoSeal VCS sa žicama vodičima koje se distribuiraju na tržištu EU.                                                                                                                                                                                               | <ul style="list-style-type: none"> <li>126 anketa</li> <li>7 ustanova</li> <li>5 zemalja</li> <li>14. novembar 2023. – 11. jun 2024.</li> <li>Lekar specijalista: <ul style="list-style-type: none"> <li>Vaskularna hirurgija</li> <li>Interventna radiologija</li> <li>Angiologija</li> </ul> </li> </ul>        | <b>Procene sredstva na skali 5 – Iskazi iz anketa</b> <ul style="list-style-type: none"> <li>Kriterijumi za prihvatanje <ul style="list-style-type: none"> <li>Ocene 3–5 se smatraju povoljnim</li> <li>Svi iskazi bi trebalo da imaju <math>\geq 80\%</math> pozitivnih povratnih informacija</li> <li>Ako se u ovoj anketi pojave neželjeni događaji, to bi trebalo da budu oni koje predviđa upravljanje rizicima.</li> </ul> </li> <li>Demografija pacijenta <ul style="list-style-type: none"> <li>Žene: 29,4% (37/126)</li> <li>Muškarci: 69,8% (88/126)</li> <li>Pol nije naveden: 0,8 (1/126)</li> </ul> </li> </ul> |

| Završene aktivnosti kliničkog praćenja nakon plasiranja na tržište |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|--------------------------------------------------------------------|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                    |  |  |  |  | <ul style="list-style-type: none"> <li>○ Starost &gt; 75 godina: 31,7%</li> <li>• Ishodi <ul style="list-style-type: none"> <li>○ Žica vodič isporučena sa FemoSeal™ VCS: 101/126 (80,2%).</li> <li>○ Trajanje procedure (minuti): 63,4 (36,6) (srednje (SD)); 57,0 (36,0-81,0) (srednje (IQR))</li> <li>○ Sve ocene performansi sistema FemoSeal™ VCS su bile povoljne.</li> <li>○ Sve ocene žice vodiča isporučene sa FemoSeal™ VCS bile su povoljne.</li> <li>○ Jedan (0,8%) neželjeni događaj: FemoSeal™ VCS diskovi nisu bili dobro poravnati verovatno zato što je potrebna ručna kompresija za postizanje hemostaze usled korišćenja čvrste žice vodiča (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 inča).</li> </ul> </li> </ul> |

Kompanija Terumo Medical Corporation je tokom aktuelnog perioda izveštavanja (1. septembar 2019. – 31. avgust 2024.) završila tri kvalitetne ankete za korisnike lekare.

Kliničke ankete za FemoSeal™ su sakupile proaktivne kliničke podatke u vezi sa bezbednošću i performansama sredstva FemoSeal™ VCS u kliničkoj primeni. Anketa je sadržala pitanja fokusirana uopšteno na sredstvo i povezani dodatni pribor, uključujući žicu vodiča od 0,038” i njihove direktne interakcije. Kliničke ankete u vezi sa žicom vodičem su sakupile proaktivne kliničke podatke u vezi sa bezbednošću i performansama u toku kliničke primene žice vodiča od 0,038” koja se isporučuje sa FemoSeal™ VCS. Pitanja u anketi su bila fokusirana naročito na



opštu primenu žice vodiča od uvođenja kroz košuljicu za izvođenje procedure u vaskulaturu do uklanjanja žice.

FemoSeal™ VCS i žica vodič od 0,038" priložena uz sredstvo su dobili prihvatljive ocene i šest (6) pritužbi je podneto za sredstvo i devet (9) komentara koji nisu bili pritužbe za žicu vodiča na osnovu procene komentara dobijenih u kvalitetnim kliničkim anketama. Pritužbe su procenjene i za FemoSeal i za žicu vodiča i ocenjene su kao deo procesa nadzora kompanije Terumo nakon plasiranja na tržište. Nisu identifikovani novi rizici ili nivoi rizika.

Anketa za korisnike lekare završena je 2024. u okviru aktivnosti PMCF-a. Rezultati ankete su pokazali da su ocena performansi i bezbednost FemoSeal™ VCS u celosti bili veoma povoljni. Takođe je demonstrirana kompatibilnost žica vodiča koje se ne isporučuju standardno sa FemoSeal™ VCS.

#### **1.4.3.2 Tekuće/planirano kliničko praćenje nakon plasiranja na tržište**

TMC ima jednu tekuću/planiranu aktivnost kliničkog praćenja nakon plasiranja na tržište. Sprovede se klinička anketa radi prospektivnog sakupljanja povratnih informacija o upotrebi žica vodiča sa sredstvom FemoSeal VCS koje se distribuiraju na tržištu EU. Anketu će sprovedi lekari da bi se proučilo koje žice vodiče su koristili u toku procedure. Svrha ove ankete je da se ispravi nedostatak koji je identifikovan kao nedostatak literature i komentara spoljnih recenzenata o kompatibilnosti sistema FemoSeal™ VCS sa upotrebom drugih žica vodiča brendova koji nisu Terumo. Povratne informacije obuhvataju tehničke ishode, kliničke performanse i bezbednost u vezi sa performansama sredstva sa različitim žicama vodičima.

#### **1.4.4 Sažetak podataka iz sistematskog pregleda literature**

Kompanija Terumo Medical Corporation sprovodi sistematske analize literature da bi sakupila i procenila kliničke podatke o bezbednosti i performansama iz objavljenih studija za sredstvo FemoSeal™ VCS i/ili slična sredstva. Cilj godišnjeg pregleda objavljene literature je identifikovanje ranije nepoznatih neželjenih dejstava, praćenje poznatih pratećih dejstava, identifikovanje pojave rizika i identifikovanje moguće sistematske pogrešne upotrebe ili upotrebe sredstva FemoSeal™ VCS suprotno oznakama.

Najnoviji pregled sistematske literature, koji je obuhvatio period od 1. septembra 2019. do 31. avgusta 2024, identifikovao je 29 objavljenih studija koje su pružile kliničke podatke o bezbednosti i performansama sredstva FemoSeal™ VCS. U devet studija prijavljeno je dvadeset tri reference o upotrebi FemoSeal™ VCS u skladu sa specifikacijom, a upotreba mimo specifikacija je prijavljena u devet studija. U načelu, pregled literature studija koje se odnose na primenu sredstva FemoSeal™ VCS pokazuju populaciju iz studije koja je reprezentativna za pacijente u EU koji se podvrgavaju procedurama perkutane vaskularne kateterizacije. Pogledajte **odjeljak 3** za listu ove 23 publikacije za upotrebu u skladu sa specifikacijom sa stručnom recenzijom.

Kliničke performanse su ocenjene na osnovu sledećih mera:

- Vreme do hemostaze je bolje od ili uporedivo sa najboljim metodama za perkutano zatvaranje zajedničke femoralne arterije.
- Vreme do ambulacije je bolje od ili uporedivo sa najboljim metodama perkutanog zatvaranja zajedničke femoralne arterije.
- Stopa javljanja postoperativnih komplikacija je uporedivo sa ili manje od aktuelnih standarda nege.

Na osnovu ovih mera kliničkih performansi, podaci u ovom pregledu literature su pokazali da sredstvo FemoSeal™ VCS može uspešno da se koristi za zatvaranje punkcije femoralne arterije (arteriotomija) kod pacijenata koji su podvrgnuti perkutanoj kateterizaciji sa košuljicom za izvođenje procedure od 7 Fr ili manjom. Potpuna hemostaza je postignuta kod većine pacijenata (79,65%–100%) i povezana je sa srednjim vremenom do hemostaze od 0,5 minuta, srednjim vremenom do otpuštanja 3 dana. Između 69,2%–86,7% pacijenata bilo je u stanju da se kreće 5 sati nakon zatvaranja, sa srednjim vremenom postoperativnog odmora od 349 minuta. Neuspeh FemoSeal™ VCS je primećen u 3,68%–4% slučajeva, a dodatna ručna kompresija je bila potrebna u 0,9%–4,4% procedura.

Klinička bezbednost je procenjena na osnovu neželjenih događaja uključujući, ali ne isključivo:

- Krvarenje
- Hematom
- Pseudoaneurizma
- Modrica
- Arteriovenska fistula
- Infekcija
- Smrt

Za svaki od ovih neželjenih događaja, prijavljena stopa javljanja za FemoSeal™ VCS u obuhvaćenim studijama je bila manja ili uporediva sa istorijski prijavljenim stopama za ručnu kompresiju i druga sredstva za zatvaranje krvnih sudova.

Nisu identifikovani neželjeni događaji kroz pregled 10 sažetaka o slučaju, jer nisu identifikovani novi, neočekivani, nastajući ili neprihvatljivi rizici.

Ukupna efikasnost korišćenja FemoSeal™ VCS tokom dijagnostičke angiografije ili interventnih operacija zavisi od više faktora kao što su: pol, starost, anatomija pacijenta, komorbiditeti, anatomsko pozicioniranje mesta punkcije, iskustvo hirurga, metod postavljanja VCD-a, postoperativna nega itd. Pored tehničkog uspeha, uključujući postizanje hemostaze, FemoSeal™ VCS je pružao kliničke koristi u vezi sa zatvaranjem vaskularnog sistema nakon punkcije

femoralne arterije, kao što je skraćanje vremena do hemostaze, skraćanje vremena do pokretljivosti. Rezultati performansi sredstvo FemoSeal™ VCS su u skladu sa onima koji se očekuju za ovu vrstu sredstava kada se koriste u skladu sa namenom. Neke reference preuzete tokom aktuelnog perioda pretrage pokazuju upotrebu predmetnog sredstva na anatomskoj lokaciji koja nije zajednička femoralna arterija i za zatvaranje arteriotomija > 7 Fr, što se smatra upotrebom koja nije u skladu sa namenom.

Tokom pregleda nisu identifikovana nepoznata neželjena dejstva, nastali rizici ili moguća sistematska pogrešna upotreba sredstva. Međutim, ako FemoSeal™ VCS pažljivo koriste obučeni lekari, medicinsko sredstvo funkcioniše kao korisno i neophodno kliničko sredstvo. Ciljana terapija, a stoga i FemoSeal™ VCS, u načelu ispunjava kliničke potrebe koje trenutno postoje u lečenju komplikacija povezanih sa vaskularnim pristupom.

Ukupno gledano, podaci u ovom pregledu literature nisu identifikovali probleme sa performansama i bezbednošću u kliničkom okruženju koji su ranije bilo nepoznati ili neželjena dejstva koja su je desila u većem broju od očekivanog/prihvatljivog. Zato se iz ovog pregleda literature može zaključiti da se sredstvo FemoSeal™ VCS, kada se koristi za pružanje kompresije za hemostazu kod arteriotomije nakon perkutane kateterizacije, i dalje se ponaša kao što je očekivano i ne povezuje se sa ozbiljnim bezbednosnim događajima.

#### 1.4.5 Sažetak podataka iz praćenja nakon plasiranja na tržište

Uspostavljen je proaktivni PMS sistem i završena je analiza svih pritužbi na mesečnom nivou i u skladu sa internim postupcima proizvodnje. Podaci o pritužbama su analizirani u periodu od 1. septembra 2019. do 31. avgusta 2024. godine. Ukupno gledano, bilo je 28 izveštaja o vigilanci medicinskih sredstava (MDV) i proizvođaču je podneto 476 pritužbi. Od 28 MDV izveštaja, 27 je bilo vezano za neželjene događaje, a jedan za kvar sredstva. Došlo je do dva smrtna ishoda tokom perioda izveštavanja, ali ni za jedan od prijavljenih smrtnih ishoda nije dokazano da ima veze sa predmetnim sredstvom. Od 476 pritužbi podnetih proizvođaču, najčešći razlozi za pritužbe bili su poteškoće u postavljanju (146 pojava, 0,0142% učestalosti). Režim otkazivanja događaja povlačenja je drugi najčešći sa učestalošću od 0,0126% (130 događaja).

FemoSeal™ Vascular Closure System je prodat u preko 1.030.136 komada širom sveta i 827.843 u Evropskom ekonomskom prostoru. Izračunata učestalost pritužbi na osnovu prodaje na globalnom nivou je 0,046%. Ukupna stopa pritužbi kupaca je veoma niska. Nisu identifikovani novi rizici koji nisu obuhvaćeni Uputstvom za upotrebu i dokumentacijom o rizicima.

Stope javljanja neželjenih pratećih dejstava su prikazane u **tabeli 1.2**. Kroz pritužbe nisu uočeni neočekivani, nastajuć ili neprihvatljivi rizici. Nije došlo do značajnog povećanja učestalosti ili ozbiljnosti poznatih neželjenih dejstava.

#### 1.4.6 Ukupan rezime kliničke performanse i bezbednosti

Sredstvo FemoSeal™ VCS je indikovano za zatvaranje punkcije zajedničke femoralne arterije (arteriotomije) kod pacijenata koji su podvrgnuti perkutanoj kateterizaciji sa košuljicom za izvođenje procedure od najviše 7 F (2,33 mm). Ova klinička procena zasniva se na sveobuhvatnoj analizi dostupnih kliničkih podataka pre i posle plasiranja na tržište i literature relevantne za namenu sredstva FemoSeal™ VCS.

Sveobuhvatna analiza objavljene literature sprovedena je u periodu od 1. septembra 2019. do 31. avgusta 2024. Dokazi su obuhvatili 29 studija za FemoSeal™ VCS. Dokazi pruženi u kliničkoj proceni zaključuju da je predmetno sredstvo bezbedno i efikasno kada se koristi u skladu sa indikacijama, a svi rizici ili neželjena prateća dejstva koji mogu da budu povezani sa sredstvom u normalnim uslovima upotrebe predstavljaju prihvatljive rizike kada se uporede u odnosu na koristi za pacijenta. Rezultati performansi za predmetna sredstva su u skladu sa onima koji se očekuju za ovu vrstu sredstava kada se koriste u skladu sa namenom.

Potencijalni neželjena prateća dejstva koja se povezuju sa upotrebom sredstva FemoSeal™ VCS obuhvataju neželjene događaje koji se obično prijavljuju kod alternativnih načina zatvaranja arteriotomije, npr. krvarenje i hematom. U načelu, stope javljanja neželjenih događaja koji su prijavljeni kod upotrebe sredstva FemoSeal™ VCS su slične stopama prijavljenim za ručnu kompresiju i slična sredstva za zatvaranje mesta vaskularnog pristupa. Precizno, za krvarenje i hematom, prijavljene stope za sredstvo FemoSeal™ VCS su manje od prijavljenih stopa za slična sredstva za zatvaranje mesta vaskularnog pristupa. Svaki od prijavljenih neželjenih događaja, iz objavljene literature i nadzora nakon plasiranja na tržište, identifikovan je ranije (pogledajte **odjeljak 1.3**).

Postojeći podaci u vezi sa kliničkom bezbednošću i performansama ukazuju na to da koristi za pacijente od upotrebe ovog sredstva za zatvaranje vaskularnog pristupa nadmašuju moguće rizike kada se koristi u skladu sa Uputstvom za upotrebu.

Kao što je navedeno u prethodnim odeljcima, pruženi podaci za sredstvo FemoSeal™ VCS pokazuje doslednost između podataka u vezi sa sredstvom koje se evaluira (npr. korišćenje sredstva, bezbednosni ishodi, kliničke performanse i kliničke koristi), identifikovanim ekvivalentnim sredstvima i podacima u vezi sa sličnim sredstvima navedenim u najnovijim dostignućima.

Unakrsna analiza bezbednosnih podataka nije identifikovala nepodudaranja između sledećeg:

- Podaci navedeni u najnovijim dostignućima
- Podaci specifični za sredstvo koje se evaluira
- Podaci navedeni u datoteci/datotekama Upravljanje rizicima

- Podaci navedeni na oznaci i/ili u Uputstvu za upotrebu (tj. obrađeni su rezidualni rizici koje treba preneti korisniku).

Kliničku bezbednost su pokazale niske stope komplikacija identifikovane u objavljenoj kliničkoj literaturi sa stručnom recenzijom, kliničkim studijama koje je sponzorirala kompanija, analizi podataka nakon plasiranja na tržište u kombinaciji bez povlačenja sa tržišta. Nisu identifikovani problemu u performansama, analizirana literatura je sadržala upotrebu ispitivanog sredstva FemoSeal™ VCS koja je dosledna sa namenom koju je definisao proizvođač.

### 1.5 Moguće dijagnostičke terapijske alternative

Ručna kompresija se standardno koristi za postizanje hemostaze na mestu arteriotomije nakon vaskularnih kateterizacija. Ručna kompresija se dovodi u vezu sa imobilizacijom pacijenta u dužem vremenskom periodu (do 8 sati nakon procedure) i znatnim osećajem nelagode i produženim boravkom u bolnici. Nedavni sistematski pregled je otkrio da je srednje vreme do postizanja hemostaze kod ručne kompresije iznosilo 20,8 minuta.<sup>1</sup>

Alternative ručnoj kompresiji obuhvataju spoljna hemostatska sredstva koja primenjuju mehaničku kompresiju na mesto arteriotomije. Ova sredstva ne skraćuju vreme do postizanja hemostaze ili vreme do ambulacije, ali smanjuju zahteve u pogledu angažovanja osoblja jer ručnu kompresiju menjaju mehaničkom kompresijom. Stope javljanja neželjenih događaja povezanih sa upotrebom mehaničke kompresije su slične stopama za ručnu kompresiju.

Sredstva za zatvaranje krvnih sudova, kao što je FemoSeal™ VCS, dizajnirana su za zatvaranje arteriotomije. Cilj je da se skрати vreme do hemostaze i omogući ranija ambulacija. Nedavni sistematski pregled, koji je obuhvatio 13 komercijalno dostupnih sredstava, otkrio je da je srednje vreme do postizanja hemostaze sredstava za zatvaranje krvnih sudova iznosilo 5,4 minuta. Srednje vreme do postizanja hemostaze za pojedinačna sredstva za zatvaranje krvnih sudova je bilo u rasponu od 1 minuta (FemoSeal™ VCS) do 14 minuta; kod većine sredstava iznosilo je između 4 i 10 minuta.<sup>1</sup>

Najčešće prijavljeni neželjeni događaji povezani sa zatvaranjem mesta arteriotomije, sa ručnim kompresijama, spoljašnjim hemostatskim sredstvima ili sredstvima za zatvaranje krvnih sudova, obuhvataju hematoma, krvarenje na mestu pristupa, pseudoaneurizmu, arteriovensku fistulu i infekciju. Isti sistematski pregled (34 randomizovana kontrolisana ispitivanja, 14.401 pacijent) otkrilo je da su stope javljanja neželjenih događaja bile slične kod ručne kompresije i upotrebe sredstava za zatvaranje krvnih sudova, a jedina razlika je bila to što je krvarenje bilo malo obilnije kod sredstava za zatvaranje krvnih sudova.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Predloženi profil korisnika i obuka

Predviđeni korisnici sredstva FemoSeal™ Vascular Closure System su lekari sa obukom koja ih kvalifikuje za izvođenje arterijskog pristupa i zatvaranja kod endovaskularnih procedura preko zajedničke femoralne arterije i koji učestvuju u programu za obuku lekara za FemoSeal™ kompanije Terumo Medical Corporation.

## 1.7 Relevantni harmonizovani i opšti standardi

| Referentni broj standarda | Tekuća godina usklađenosti/revizija | Opis                                                                                                                                     |
|---------------------------|-------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070                 | 2014/AMD1:2018                      | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070              | 2014/A1:2018                        | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance              | 20. maj, 2021.                      | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052                | 2015.                               | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213                | 2017.                               | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503                | 2020.                               | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182                | 2019.                               | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |
| EN ISO 13485              | 2016/A11:2021                       | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 13485                 | 2016.                               | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |

| Referentni broj standarda | Tekuća godina usklađenosti/revizija | Opis                                                                                                                                                                     |
|---------------------------|-------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14644-1               | 2015.                               | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1            | 2015.                               | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2               | 2015.                               | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2            | 2015.                               | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3               | 2019.                               | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3            | 2019.                               | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1               | 2003.                               | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1            | 2003.                               | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2               | 2003/TC1:2004                       | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| EN ISO 14698-2            | 2003/TC 1:2004                      | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| USP <788>                 | ne postoji                          | PARTICULATE MATTER IN INJECTIONS                                                                                                                                         |



| Referentni broj standarda | Tekuća godina usklađenosti/revizija | Opis                                                                                                                 |
|---------------------------|-------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| EU farmakopeja 2.9.19     | ne postoji                          | Particulate Contamination: Sub-Visible Particles                                                                     |
| IEC 62366-1               | 2015.                               | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN 62366-1                | 2015.                               | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN ISO 14971              | 2019/A11:2021                       | Medical devices — Application of risk management to Medical devices                                                  |
| ISO 14971                 | 2019.                               | Medical devices — Application of risk management to Medical devices                                                  |
| ASTM F1980                | 2016.                               | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1            | 2020.                               | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1               | 2018.                               | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2            | 2006.                               | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2               | 2006.                               | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3            | 2014.                               | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3               | 2014.                               | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4            | 2017.                               | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4               | 2017.                               | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |



| Referentni broj standarda | Tekuća godina usklađenosti/revizija | Opis                                                                                                                                       |
|---------------------------|-------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-5            | 2009.                               | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                                         |
| ISO 10993-5               | 2009.                               | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                                         |
| EN ISO 10993-6            | 2016.                               | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| ISO 10993-6               | 2016.                               | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| EN ISO 10993-10           | 2023.                               | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| ISO 10993-10              | 2021.                               | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| EN ISO 10993-11           | 2018.                               | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| ISO 10993-11              | 2017.                               | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| EN ISO 10993-12           | 2021.                               | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| ISO 10993-12              | 2021.                               | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| EN ISO 10993-17           | 2009.                               | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17              | 2002.                               | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18              | 2020/A1:2022                        | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |

| Referentni broj standarda | Tekuća godina usklađenosti/revizija | Opis                                                                                                                                                                         |
|---------------------------|-------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 10993-18           | 2020/A1:2022                        | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-23           | 2021.                               | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23              | 2021.                               | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382                | 2018.                               | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756                 | 2017.                               | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>                  | ne postoji                          | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>                 | ne postoji                          | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72            | 2019.                               | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135              | 2014/A1:2019                        | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135                 | 2014/A1:2018                        | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7            | 2008/A1:2022                        | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |
| ISO 10993-7               | 2008/A1:2019                        | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                                            |

| Referentni broj standarda | Tekuća godina usklađenosti/revizija | Opis                                                                                                                                                            |
|---------------------------|-------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN 556-1                  | 2024.                               | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices |
| EN ISO 11737-1            | 2018/A1:2021                        | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11737-1               | 2018/A1:2021                        | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| EN ISO 11138-1            | 2017.                               | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-1               | 2017.                               | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| EN ISO 11138-2            | 2017.                               | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 11138-2               | 2017.                               | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| EN ISO 15223-1            | 2016.                               | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| ISO 15223-1               | 2016.                               | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| EN 1041                   | 2008/A1:2013                        | Information supplied by the manufacturer of medical devices                                                                                                     |
| EN ISO 11607-1            | 2020/A1:2023                        | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                         |

| Referentni broj standarda | Tekuća godina usklađenosti/revizija | Opis                                                                                                                                                                       |
|---------------------------|-------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11607-1               | 2019/A1:2023                        | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems                                    |
| EN ISO 11607-2            | 2020/A1:2023                        | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ISO 11607-2               | 2019/A1:2023                        | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169                | 2016.                               | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M         | 2016.                               | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825                | 2018.                               | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096                | 2011. (R 2019)                      | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M             | 2015.                               | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24              | 2021.                               | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3               | 2020.                               | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |
| MDCG 2020-8               | 2020.                               | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                             |
| MDCG 2020-7               | 2020.                               | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                          |

| Referentni broj standarda | Tekuća godina usklađenosti/revizija | Opis                                                                                                                                                                                                                                                          |
|---------------------------|-------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2020-6               | 2020.                               | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                                                                                                          |
| MDCG 2019-9 v1            | 2022.                               | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                                                                                      |
| MDCG 2019-8 v2            | 2020.                               | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15              | 2020.                               | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11              | 2021.                               | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19              | 2021.                               | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4            | 2021.                               | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2               | 2019.                               | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1               | 2019.                               | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7               | 2018.                               | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6               | 2018.                               | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |

| Referentni broj standarda | Tekuća godina usklađenosti/revizija | Opis                                                                                                                                                                                          |
|---------------------------|-------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2018-4               | 2018.                               | MDCG 2018-4 Annex: UDI database<br>Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                               |
| MDCG 2018-3<br>v1         | 2020.                               | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25              | 2021.                               | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2.12-2<br>Rev 2    | 2012.                               | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                        |

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### 3.0 ISTORIJA REVIZIJA

| SSCP broj revizije        | Datum objavljivanja | Opis izmene                                                    | Reviziju je potvrdilo notifikovano telo                                                                                                                                                                                                                                                                         |
|---------------------------|---------------------|----------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022              | 20. januar 2023.    | Prvo izdanje, nakon MDR CE sertifikovanja                      | <p><input checked="" type="checkbox"/> Da</p> <p>Jezik validacije: English</p> <p><input type="checkbox"/> Ne (odnosi se samo na klasu IIa ili neka implantabilna sredstva klase IIb (MDR, član 52 (4) 2. pasus) za koji NT još uvek nije potvrdilo SSCP)</p> <p><input type="checkbox"/> Drugo (navedite):</p> |
| SSCP-FS-2023 – Revizija 1 | 15. mart 2024.      | Ažurirano za period od 1. januara 2019. do 31. decembra 2023.  | <p><input checked="" type="checkbox"/> Da</p> <p>Jezik validacije: English</p> <p><input type="checkbox"/> Ne (odnosi se samo na klasu IIa ili neka implantabilna sredstva klase IIb (MDR, član 52 (4) 2. pasus) za koji NT još uvek nije potvrdilo SSCP)</p> <p><input type="checkbox"/> Drugo (navedite):</p> |
| SSCP-FS-2024 Revizija 1   |                     | Ažurirano za period od 1. septembra 2019. do 31. avgusta 2024. | <p><input type="checkbox"/> Da</p> <p>Jezik validacije: English</p> <p><input type="checkbox"/> Ne (odnosi se samo na klasu IIa ili neka implantabilna sredstva klase IIb (MDR, član 52 (4) 2. pasus) za koji NT još uvek nije potvrdilo SSCP)</p> <p><input type="checkbox"/> Drugo (navedite):</p>            |
| SSCP-FS-2024 Revizija 2   | June 20, 2025       | Revidirano na osnovu upita NSAI za validaciju                  | <p><input checked="" type="checkbox"/> Da</p> <p>Jezik validacije: English</p> <p><input type="checkbox"/> Ne (odnosi se samo na klasu IIa ili neka implantabilna sredstva klase IIb (MDR, član</p>                                                                                                             |

|  |  |  |                                                                                                                |
|--|--|--|----------------------------------------------------------------------------------------------------------------|
|  |  |  | 52 (4) 2. pasus) za koji NT još<br>uvek nije potvrdilo SSCP)<br><br><input type="checkbox"/> Drugo (navedite): |
|--|--|--|----------------------------------------------------------------------------------------------------------------|

## Sammanfattning av säkerhet och kliniska prestanda

### FemoSeal™ Vascular Closure System

|                                         |                                                                                              |
|-----------------------------------------|----------------------------------------------------------------------------------------------|
| <b>Tillverkare</b>                      | Terumo Medical Corporation<br>265 Davidson Ave, svit 320<br>Somerset, NJ 08 873 USA          |
| <b>Tillverkarens SRN</b>                | US-MF-000019594                                                                              |
| <b>Ledningsrepresentant/PRRC</b>        | Kimberly Feitl<br>Vice President, Quality                                                    |
| <b>Grundläggande UDI-DI</b>             | 38 970FS79                                                                                   |
| <b>EMDN-nummer</b>                      | C900199 – Hemostassystem – Övrigt                                                            |
| <b>Apparatklass</b>                     | Klass III                                                                                    |
| <b>Året då enheten först CE-märktes</b> | 2005                                                                                         |
| <b>Återförsäljare EU</b>                | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgien<br>SRN: BE-AR-000001433 |
| <b>Anmält organ</b>                     | NSAI<br>CE 0050                                                                              |

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Denna sammanfattning av säkerhet och klinisk prestanda ska ge allmänheten tillgång till en uppdaterad sammanfattning av de viktigaste aspekterna av säkerhet och kliniska prestanda för FemoSeal™ Vascular Closure System (VCS).

En sammanfattning av enhetens säkerhet och kliniska prestanda, avsedd för användare/sjukvårdspersonal ges nedan i **avsnitt 1.0**.

## **1.0 SAMMANFATTNING FÖR ANVÄNDARE/SJUKVÅRDSPERSONAL**

Sammanfattningen är inte avsedd att ersätta den bruksanvisning som utgör huvuddokumentet för att säkerställa säker användning av enheten, och är inte heller avsedd att ge förslag gällande diagnostik eller behandling till avsedda användare eller patienter. SSCP är inte avsedd att ersätta den obligatoriska informationen på implantatkorten eller i andra obligatoriska dokument.

### **1.1 Avsedd användning av enheten**

#### **1.1.1 Avsedd användning**

FemoSeal™ Vascular Closure System är en medicinteknisk produkt för förslutning av en arteriell punktion efter perkutan kateterisering genom den gemensamma femoralartären.

#### **1.1.2 Indikationer för användning**

FemoSeal™ Vascular Closure System är indicerat för användning vid förslutning av den vanliga femorala arteriella punktionen (arteriotomi) hos patienter som har genomgått perkutan kateterisering med hjälp av en ingreppshylsa på 2,33 mm (7F) eller mindre.

#### **1.1.3 Kontraindikationer och/eller begränsningar**

FemoSeal™ Vascular Closure System är kontraindicerat för patienter med arteriotomier där hylsor eller enheter som är större än 2,33 mm (7F) har använts.

#### **1.1.4 Avsedda patientpopulationer**

Säkerheten och effektiviteten hos FemoSeal™ Vascular Closure System har fastställts hos patienter från 18 års ålder som har genomgått perkutan kateterisering med en ingreppshylsa som är 2,33 mm (7F) eller mindre.

#### **1.1.5 Särskilda patientpopulationer**

Säkerhet och effektivitet för FemoSeal™ Vascular Closure System har inte fastställts för följande patientpopulationer:

- Patienter med befintlig autoimmun sjukdom.
- Patienter som genomgår terapeutisk trombolys.
- Patienter med kliniskt signifikant perifer kärlsjukdom.
- Patienter med okontrollerad hypertoni (> 220 mmHg systoliskt eller > 110 mmHg diastoliskt).
- Patienter med blödningsrubbning, inklusive trombocytopeni (trombocytvärde <100 000), eller anemi (Hgb <10 mg/dl).



- Patienter med en innerlumen i den femorala artären som är mindre än 5 mm.
- Patienter med nedsatt njur- och/eller leverfunktion.
- Patienter med annan relevant komorbiditet.
- Population med specifikt ras och/eller etniskt ursprung.
- Patienter med hjärtinfarkt inom 72 timmar.
- Patienter med kärltransplantat eller stent vid punktionsstället.
- Patienter som är gravida eller ammar.
- Patienter under 18 år.

### 1.1.6 Avsedda användare

De avsedda användarna av FemoSeal™ Vascular Closure System är läkare med utbildning som kvalificerar dem att utföra arteriell åtkomst och förslutning för endovaskulära ingrepp genom den gemensamma femoralartären och har deltagit i ett läkarinstruktionsprogram från Terumo Medical Corporation FemoSeal™.

## 1.2 Enhetsbeskrivning

### 1.2.1 Beskrivning av enheten

FemoSeal™ Vascular Closure System, tillverkat av Terumo Medical Corporation (TMC), är en resorberbar kärlförslutningsenhet utformad för att uppnå femoral arteriell hemostas efter perkutan kateterisering genom den gemensamma femoralartären.

FemoSeal™ förslutningselement består av två resorberbara polymerskivor, en inre tätning och en yttre låsskiva, som hålls samman av resorberbar multifilamenttråd och därigenom mekaniskt försluter arteriotomin (se **Figur 1.1** och **Figure 1.2**). När den yttre låsskivan har fällts ut genom den konformade hylsan pressas den fast på multifilamentaxeln vilket gör att punktionsstället mellan den inre och den yttre låsskivan stängs mekaniskt. Den inre tätningen och den yttre låsskivan hålls på plats genom friktion på multifilamentaxeln. Hemostas uppnås mekaniskt. Förslutningselementen bryts ned genom hydrolys.

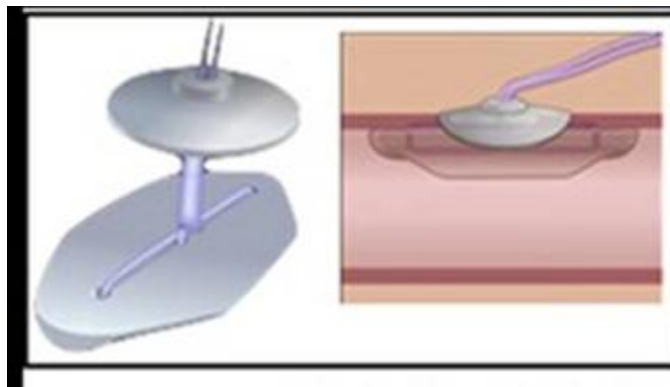
De implanterbara förslutningskomponenterna, dvs. den inre tätningen och den yttre låsskivan, bryts ned på arton (18) månader medan multifilamentet uppskattas brytas ned och absorberas via hydrolys av omgivande vävnad efter två (2) till tre (3) år. Förmågan hos de implanterbara förslutningskomponenterna att upprätthålla kompression på arteriotomin har testats i upp till åtta (8) timmar. Nedbrytningsprodukterna metaboliseras och utsöndras i urinen eller går ut som koldioxid via lungorna. Inga ackumulerings effekter har observerats i djurstudier. De ytterligare

komponenter i FemoSeal™ som kommer att komma i kontakt med levande vävnad eller blod under ingreppet är den konformade hylsan, dilatatorn, packningsröret, införaren och ledaren.

**Figur 1.1 Inre tätning respektive yttre låsskiva**

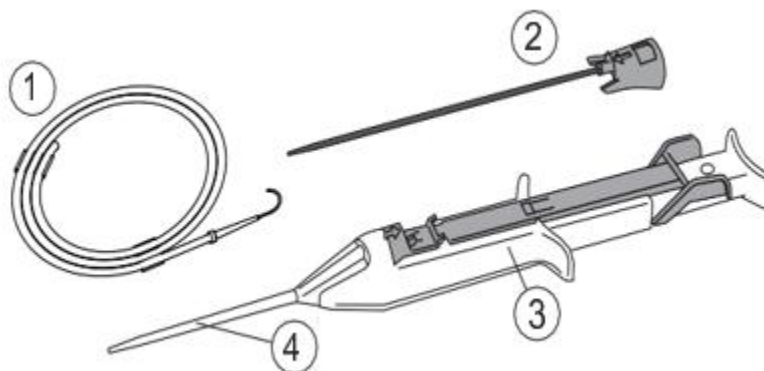


**Figur 1.2 Inre tätning och yttre låsskiva utplacerad**



FemoSeal™-enheten är förpackad tillsammans med en dilatator och en ledare med en YD på 0,97 mm (0,038 tum), en längd på 70 cm (27,5 tum) och en J-uträtare, se **figur 1.3** nedan. Ledaren är innesluten i ett polyetylenrör. Alla delar är förpackade i en styv pappersförpackning. Förpackningen innehåller även patientimplantatkortet. FemoSeal™ Vascular Closure System kräver inga ytterligare tillbehör för att enheten ska fungera som avsett, och enheten är endast avsedd att användas med dilatatorn och ledaren som ingår i produktens förpackning.

**Figur 1.3 FemoSeal™ VCS-enhet med ledare och dilatator**



### 1.2.2 Råmaterial och komponenter

I **tabell 1.1** nedan anges komponenterna i FemoSeal™ VCS.

**Tabell 1.1 Råmaterial och komponenter hos FemoSeal™ VCS**

| Artikelnummer | Beskrivning                                       |                                                   | Material                                                                                                                                                                                 |
|---------------|---------------------------------------------------|---------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1             | 0,038" (0,97 mm) ledare med J-uträtare för ledare |                                                   | Ledare: 304 Rostfritt stål<br>J-uträtare: Polypropylen, lila pigment<br>Klämma: Polyetylen<br>Slangar Polyetylen                                                                         |
| 2             | FemoSeal dilatator                                |                                                   | Fattning: Tetrahydrofuran, blått pigment, polybutylentereftalat (PBT)<br><br>Rör: Högdensitetspolyeten (HDPE), svart pigment<br><br>Smörjmedel: Silikon Dow Corning 360                  |
| 3/4           | FemoSeal-enhet                                    | Formgjuten RD7 – inre tätning och yttre låsskiva* | Sampolymer mellan glykolid, trimetylenkarbonat, e-kaprolakton och TMP: trimetylolpropan (initiator)                                                                                      |
|               |                                                   | Multifilament *                                   | Segmenterad sampolymer mellan L,L-laktid, trimetylenkarbonat, e-kaprolakton och 1,3 propanediol (initiator)<br><br>Beläggningen är sampolymer mellan glykolid, e-kaprolakton och L-lysin |

|  |  |                         |                                                 |
|--|--|-------------------------|-------------------------------------------------|
|  |  | Packningsrör            | Polypropylen                                    |
|  |  | Införare                | 304V Rostfritt stål                             |
|  |  | Sprutkolvshuvudshållare | Polybutylentereftalat (PBT)                     |
|  |  | Hus                     | Polybutylentereftalat (PBT)                     |
|  |  | Knapp                   | Polybutylentereftalat (PBT)                     |
|  |  | Knapplock               | Polyoxymetylen (POM)/polyacetalsampolymer       |
|  |  | Hylsa                   | Polybutylentereftalat (PBT)                     |
|  |  | Distans                 | Polybutylentereftalat (PBT)                     |
|  |  | Kona                    | Polypropylen                                    |
|  |  | Husets lock             | Polybutylentereftalat (PBT)                     |
|  |  | Säkerhetsspärr          | Polybutylentereftalat (PBT), blått pigment      |
|  |  | Hylslock                | Polybutylentereftalat (PBT)                     |
|  |  | Rörpackning             | Silikon shore A 70                              |
|  |  | Husets packning         | Silikon shore A 50                              |
|  |  | Fjäder                  | 302 Rostfritt stål                              |
|  |  | Konformad hylsa         | Polypropylen<br>Silikon Dow Corning 360, Hexane |

\* Implanterbar del av enheten; implanterbara komponenter är MR-säkra

FemoSeal™ VCS är steriliserad med etylenoxid (EO) och är en medicinteknisk produkt för engångsbruk. FemoSeal™ VCS-enheten är konstruerad på ett sådant sätt att den inte kan återanvändas.

### **Driftläge**

FemoSeal™ VCS främjar mekanisk hemostas genom implantering av förslutningselement inuti och utanför den gemensamma femorala artären. Den inre förseglingen som förseglar punktionsstället och den yttre låsbrickan som håller den inre förseglingen på plats förhindrar blödning.

### **1.2.3 Klinisk nytta**

FemoSeal™ VCS ger följande kliniska fördelar jämfört med kärlförslutning efter punktion av den gemensamma femorala artären:

- Kortare tid till hemostas<sup>1</sup>

- Kortare tid till mobilitet<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

#### 1.2.4 Tidigare generation(er) eller varianter

- Den första versionen av FemoSeal™ VCS (#11200) såldes på den europeiska marknaden under 2005 och 2006.
- Den aktuella FemoSeal™ VCS (#11202) med förbättrat leveranssystem har funnits på marknaden sedan 28 mars 2006.

#### 1.2.5 Tillbehör avsedda att användas i kombination med enheten

FemoSeal™-enheten är förpackad tillsammans med en dilatator, en 0,97 mm (0,038") OD, en 70 cm (27,5") lång ledare och en J-uträtare. Ledaren är ett tillbehör till FemoSeal™-enheten. J-uträtaren är en komponent i ledaren, medan dilatatorn är en komponent i FemoSeal™-enheten. Ledaren är den enda komponent som anses vara ett tillbehör. Ledaren är innesluten i ett polyetylenrör. Alla delar är förpackade i en styv pappersförpackning. Förpackningen innehåller även patientimplantatkortet. FemoSeal™ Vascular Closure System kräver inga ytterligare tillbehör för att enheten ska fungera som avsett, och enheten är endast avsedd att användas med dilatatorn och ledaren som ingår i produktens förpackning.

#### 1.2.6 Andra enheter och produkter som är avsedda att användas i kombination med enheten

FemoSeal™ VCS kräver inga ytterligare enheter för att fungera som avsett.

### 1.3 Risker och varningar

#### 1.3.1 Kvarstående risker och oönskade effekter

Kända eller förutsebara biverkningar, skador och komplikationer i samband med användning av FemoSeal™ VCS till följd av kvarstående risk listas i **tabell 1.2**. Frekvensen baseras på en analys av riskdokumentationen och beräknas utifrån data från övervakning efter marknadsintroduktion från 1 januari 2019 till 31 augusti 2024. Det finns inga okända restrisker för FemoSeal™ VCS och alla tillämpliga risker har hanterats genom bruksanvisningen och riskhanteringsprocessen.

**Tabell 1.2. Biverkningar/komplikationer med FemoSeal**

| Skada                                      | Förekomst (%) | Risikförebyggande faktorer                                                                                                                                                   |
|--------------------------------------------|---------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Allergisk reaktion                         | 0,0000        | Åtgärder och planer för att minska riskerna så långt som möjligt har behandlats genom produktdesignegenskaper, tillverkningsriktlinjer, produktmärkning och läkarutbildning. |
| Aneurysm                                   | 0,0000        |                                                                                                                                                                              |
| AV-fistel                                  | 0,0001        |                                                                                                                                                                              |
| Blodförlust/blödning                       | 0,0280        |                                                                                                                                                                              |
| Dödsfall                                   | 0,0002        |                                                                                                                                                                              |
| Ekkymos                                    | 0,0000        |                                                                                                                                                                              |
| Emboli                                     | 0,0000        |                                                                                                                                                                              |
| Främmandekroppsreaktion                    | 0,0000        |                                                                                                                                                                              |
| Hematom                                    | 0,0027        |                                                                                                                                                                              |
| Blödning                                   | 0,0001        |                                                                                                                                                                              |
| Infektion                                  | 0,0002        |                                                                                                                                                                              |
| Inflammatorisk reaktion                    | 0,0000        |                                                                                                                                                                              |
| Domning                                    | 0,0000        |                                                                                                                                                                              |
| Smärta                                     | 0,0000        |                                                                                                                                                                              |
| Obehag för patienten                       | 0,0004        |                                                                                                                                                                              |
| Fördröjning av procedur                    | 0,0065        |                                                                                                                                                                              |
| Pseudoaneurysm                             | 0,0004        |                                                                                                                                                                              |
| Retroperitoneal blödning                   | 0,0002        |                                                                                                                                                                              |
| Sepsis                                     | 0,0000        |                                                                                                                                                                              |
| Tromboemboli                               | 0,0000        |                                                                                                                                                                              |
| Trombos                                    | 0,0001        |                                                                                                                                                                              |
| Kärlocklusion/ischemi i nedre extremiteter | 0,0002        |                                                                                                                                                                              |
| Kärlperforation                            | 0,0000        |                                                                                                                                                                              |
| Dissektion/laceration av kärlvävnad        | 0,0003        |                                                                                                                                                                              |

### 1.3.2 Varningar och försiktighetsåtgärder

#### Varningar

1. Använd inte produkten om förpackningen är skadad eller om den sterila barriären inte är intakt.
2. Använd inte efter utgångsdatum – de biologiskt nedbrytbara komponenterna kanske inte fungerar som de ska.
3. Använd inte produkten om någon del verkar skadad eller defekt på något sätt.
4. Användning av FemoSeal™ Vascular Closure System där bakteriell kontaminering av ingreppshylsan eller omgivande vävnad kan ha inträffat kan orsaka infektion.
5. Om det misstänks att den bakre arteriella väggen har punkterats eller mer än en arteriell punktion har gjorts ska du inte förlita dig enbart på FemoSeal™ Vascular Closure System för att uppnå arteriell hemostas. Använd ytterligare manuell eller mekanisk kompression.
6. Om punktionsstället är vid eller placerat distalt om den femorala artärens bifurkation ska FemoSeal™ Vascular Closure System inte användas på grund av risken för felaktig placering av den inre förseglingen. Detta kan leda till blödningskomplikationer och/eller störningar i det normala blodflödet.
7. Vid ihållande arteriell blödning från incisionsstället ska multifilamentet inte klippas till förrän hemostas har uppnåtts. Om hemostas inte uppnås, fäst multifilamentet med ett sterilt sårförband och applicera kompletterande kompression tills hemostas uppnås. Vid ihållande arteriell blödning kan betydande blödningskomplikationer uppstå, vilket kan leda till patientskada eller dödsfall.
8. Använd inte FemoSeal™ Vascular Closure System om punktionsstället är proximalt om ljumskligamentet eftersom detta kan leda till retroperitonealt hematom.
9. Patienter med högre blödningsrisk kan drabbas av ökad blodförlust som kräver transfusion.
10. Om den inre skivan lossnar kan det potentiellt orsaka en trombotisk och/eller embolisk händelse.

#### Försiktighetsåtgärder

1. FemoSeal™ Vascular Closure System ska användas av läkare med adekvat utbildning i användning av enheten.
2. Utför ett begränsat femoralt angiogram eller en ultraljudsvägledd femoralpunktion innan FemoSeal™ Vascular Closure System placeras ut.
3. Avbryt proceduren om:

- Lumendiameter för femoral artär < 5 mm.
  - Stenos och/eller betydande plack förekommer i närheten av det gemensamma femorala arteriella punktionsstället.
  - Arteriell punktion är vid, eller distalt om, den femorala artärens bifurkation.
  - Avvikande förgreningar eller kärlabnormiteter förekommer i närheten av det gemensamma femorala arteriella punktionsstället.
4. Om hematom föreligger måste extra försiktighet iakttas för korrekt införande av den konformade hylsan i artären.
  5. Använd en enkelväggig punktionsmetod. Punktera inte artärens posteriora vägg.
  6. Använd alltid steril teknik vid användning av FemoSeal™ Vascular Closure System.
  7. FemoSeal™ Vascular Closure System är endast avsett för engångsbruk och ska inte omsteriliseras eller återanvändas på något sätt. FemoSeal™-enheten är utformad på ett sådant sätt att den inte kan återanvändas.
  8. Avbryt proceduren om den inre förseglingen löser ut på grund av oväntat motstånd.
  9. För korrekt placering av den inre förseglingen ska du flytta tummen så att knappen kan fjädra tillbaka fritt.
  10. Se till att spetsen på FemoSeal™-enhetens konformade hylsa är under hudytan innan den yttre låsskivan placeras ut. Den yttre låsskivan kan oavsiktligt placeras ovanför hudnivån hos patienter med ett kort avstånd mellan den femorala artären och hudnivån.
  11. För korrekt placering kan ett hudsnitt vara nödvändigt före placering.
  12. Om den inre förseglingen är inne i artären men det inte är möjligt att trycka in knappen helt och placera ut den yttre låsskivan så kan det krävas ett kirurgiskt ingrepp för att ta bort FemoSeal™ förslutningselement.
  13. Om ompunktion av samma femorala artär blir nödvändig inom 18 månader ska ompunktion göras minst en centimeter proximalt om det tidigare åtkomststället för FemoSeal™ Vascular Closure System.
  14. Instruera patienten att följa läkarens ordination om inspektion av förslutningsstället.
  15. Instruera patienten att bära patientinformationskortet under de kommande 18 månaderna

### **Försiktighetsåtgärder vid utskrivning**

Innan utskrivning övervägs ska patienten bedömas med avseende på följande kliniska tillstånd:

1. Blödning och/eller hematom vid förslutningsstället.
2. Smärta när patienten går.



3. Tecken på infektion vid förslutningsstället.

### 1.3.3 Korrigerande säkerhetsåtgärder för marknaden

Det fanns en korrigerande säkerhetsåtgärd för marknaden som omfattade FemoSeal™ VCS under perioden 1 september 2019 till 31 augusti 2024.

2022 återkallade Terumo frivilligt FemoSeal™ VCS på grund av klagomål som påstods bero på fel i process- och partifrisläppningstester av Elkton-tillverkade FemoSeal-produkter för mätning av tryckkraft och retraktionskraft. Totalt återkallades 950 enheter från Sydkorea.

## 1.4 Klinisk utvärdering och klinisk uppföljning efter marknadsintroduktion

**Tabell 1.3** innehåller en lista över de centrala studier som bidrog till att föra ut FemoSeal™ VCS på marknaden samt studier efter marknadsintroduktion och kliniska uppföljningsaktiviteter efter marknadsintroduktion. Enhetsversionen som används i studien ingår i tabellen nedan. Den första versionen av FemoSeal™ VCS (#11200) fanns på marknaden fram till 2006, medan nästa version (#C11202) släpptes på marknaden 2006 och är den produkt som för närvarande finns på marknaden.

**Tabell 1.3 Sammanfattning av centrala studier**

| Funktionell djurtestning före marknadsintroduktion                                                                                                                                                                                                                      | Enhetsversion             |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                     |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                     |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                     |
| Första kliniska studien på människa                                                                                                                                                                                                                                     |                           |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                     |
| Slutförda kliniska studier efter marknadsintroduktion                                                                                                                                                                                                                   |                           |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                                                                              | C11202<br>(aktuell enhet) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                                                                                       | C11202<br>(aktuell enhet) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                                                                                                                                                          | C11202<br>(aktuell enhet) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)                                                                                                                                                  | C11202<br>(aktuell enhet) |

| Planerade/pågående kliniska studier efter marknadsintroduktion                                                                  |                           |
|---------------------------------------------------------------------------------------------------------------------------------|---------------------------|
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                      | C11202<br>(aktuell enhet) |
| Kliniska uppföljningsaktiviteter efter marknadsintroduktion                                                                     |                           |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(aktuell enhet) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(aktuell enhet) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(aktuell enhet) |

### 1.4.1 Sammanfattning av data från djurtestning och kliniska studier före marknadsintroduktion

I tabell 1.4 nedan beskrivs samtliga förmarknadsstudier, både djurtestning och kliniska studier.

**Tabell 1.4 Sammanfattningar av förmarknadsstudier**

| Funktionell djurtestning före marknadsintroduktion                                                                                                                                                                                                                      |                                                                      |                                        |                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------|----------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Studiens namn                                                                                                                                                                                                                                                           | År/CI                                                                | Studietyp                              | Syfte                                                                                                                                                                                                                                               | Milstolpar                                                                                                                                                                                                                                                                                                                                                    | Potentiella acceptanskriterier                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 2000<br>Radi Medical System AB<br><br>Utförs av Biomatech, Frankrike | Djurstudie;<br>Explorativ undersökning | Syftet med studien var att utvärdera biokompatibiliteten och biofunktionaliteten hos ett biologiskt nedbrytbart implantat som är utformat för att uppnå hemostas i kärlsystemet. Rapport om reservdjur från studie nummer 862 (dokument nr 1051-01) | N = 3 vuxna tackor, 1 djur per tidspunkt<br><br>Uppföljning för histopatologisk analys, makroskopisk gradering och ultrastrukturell analys<br><br><ul style="list-style-type: none"> <li>12 månader</li> <li>15 månader</li> <li>18 månader</li> </ul><br>Ultraljudsuppföljning med färgdoppler – 30 dagar vid åtkomstställen i karotis- och femoralartärerna | Arteriell öppenhet <ul style="list-style-type: none"> <li>Bedömning av blodflödet efter utplacering – 2/3 blodflödesminskning associerad med temporär arteriell vasospasm som tillskrevs ingreppet, båda inträffade vid vänster gemensam karotisartär</li> <li>Ultraljudsbedömning med färgdoppler (4 veckor) - 3/3 (100 %) utan större minskning av blodflödet 30 dagar efter implantation</li> </ul><br>Makroskopiska observationer <ul style="list-style-type: none"> <li>12 månader – öppenhet bekräftades makroskopiskt genom frånvaro av anatomiskt synlig ocklusion; inga makroskopiska lokala intoleranslesioner (blödning, nekros eller neovaskularisering); inkapsling av inre skiva föreföll vara markerad</li> <li>15 månader – makroskopisk</li> </ul> |

|                                                                                                                                                 |                                                                   |                                     |                                                                                                                                                          |                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|-------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------|-------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                 |                                                                   |                                     |                                                                                                                                                          |                                                                                                                                    | <p>observation visade inga tecken på inflammation; inga rester av inre eller yttre skivor identifierade; inkapslingsvävnad i området runt den yttre skivan såg likadan ut som vid 12 månadersobservation</p> <ul style="list-style-type: none"> <li>18 månader – makroskopisk observation visade inga tecken på lokal intolerans, synlig yttre skiva (3/3 fall), nedbrytning av inre skiva komplett; 1/3 (vänster gemensam karotisartär) – depression av artärväggen observerad på implantatstället (kan ha samband med insättning av enheten)</li> </ul> <p>Slutsatser</p> <ul style="list-style-type: none"> <li>Makroskopiskt: 12, 15 och 18 månader efter implantationen upptäcktes inga tecken på nekros, degeneration eller trombos.</li> <li>Nedbrytningsprocessen för de inre och yttre skivorna verkade fortskrida mellan 12 och 18 månader och föreföll kompletta efter 18 månader, med en vitaktig vävnad som täcker implantationsområdet.</li> <li>Histologiskt sett var polymermaterialet inte längre synligt efter 18 månader, men en endoluminal fibrös vävnad fanns närvarande. Inga nekrotiska, degenerativa eller trombotiska lesioner noterades.</li> </ul> |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in | 2002 Radi Medical System AB<br><br>Utförs av Biomatech, Frankrike | Djurstudie; Explorativ undersökning | Syftet med studien var att utvärdera biokompatibiliteten hos ett biologiskt nedbrytbart implantat som är utformat för att uppnå hemostas i kärlsystemet. | Uppföljning (efter implantation) <ul style="list-style-type: none"> <li>12 veckor</li> <li>24 veckor</li> <li>36 veckor</li> </ul> | <p>Grad av öppenhet i karotis- och femoralartärer efter 4 veckor</p> <ul style="list-style-type: none"> <li>Större minskning av blodflödet 0/12 (0 %)</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |

|                                                                                                                         |  |  |  |                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-------------------------------------------------------------------------------------------------------------------------|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). |  |  |  | <p>N = 12 får, 3 djur per tidpunkt, 3 reservdjur avlivade vid 12, 15 och 18 månader</p> <p>Implantationsställen – höger och vänster femorala artär, höger och vänster gemensamma karotisartärer</p> <p>Ultraljudsanalys av färgdoppler</p> | <p><u>Ingen större minskning av blodflödet</u></p> <ul style="list-style-type: none"> <li>Kraftigt nedsatt blodflöde i samband med införande av enheten 0/12 (0 %)</li> <li>Minskat blodflöde i vänster gemensam karotis 2/12 (16,6 %) på grund av tillfällig arteriell vasospasm (tillskrivs operation, inte enheten)</li> </ul> <p><u>Försämrat blodflöde vid uppföljning</u></p> <p>12 veckor – 0/12 (0 %)</p> <p>24 veckor – 0/12 (0 %)</p> <p>36 veckor – 0/12 (0 %)</p> <p>Blodtrycksmätning (3 får – 36 veckor)</p> <ul style="list-style-type: none"> <li>Ingen större minskning av blodflödet har upptäckts</li> </ul> <p>Makroskopiska data för integration och degradering (grad 0-4)</p> <p><u>Åtkomstställen karotis</u></p> <p><u>Insida</u></p> <p>-kapsling</p> <p>12 veckor 1,3</p> <p>24 veckor 0,8</p> <p>36 veckor 0,7</p> <p>-materialnedbrytning</p> <p>12 veckor 2,2</p> <p>24 veckor 2,3</p> <p>36 veckor 0,7</p> <p><u>Utsida</u></p> <p>-kapsling</p> <p>12 veckor 2,0</p> <p>24 veckor 1,0</p> <p>36 veckor 0,8</p> <p>-materialnedbrytning</p> <p>12 veckor 2,0</p> <p>24 veckor 2,7</p> <p>36 veckor 3,2</p> <p><u>Åtkomstställen femoral artär</u></p> <p><u>Utsida</u></p> <p>-kapsling</p> |
|-------------------------------------------------------------------------------------------------------------------------|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|  |  |  |  |  | 12 veckor 1,0<br>24 veckor 2,7<br>36 veckor 1,0<br>-materialnedbrytning<br>12 veckor 2,0<br>24 veckor 2,4<br>36 veckor 3,0<br><br><i>Insida</i><br>-kapsling<br>12 veckor 2,0<br>24 veckor 1,2<br>36 veckor 1,0<br>-materialnedbrytning<br>12 veckor 1,0<br>24 veckor 2,2<br>36 veckor 3,0<br><br><u>Histologiska data för integration, nedbrytning och inflammatoriska parametrar (medelvärde av relevanta värden, index 0-4) n=6</u><br><br><u>Åtkomstställen karotis</u><br>Extern fibros<br>12 veckor – 2,3<br>24 veckor – 2,3<br>36 veckor – 1,8<br>Intern neointima<br>12 veckor – 3,0<br>24 veckor-2,7<br>36 veckor-3,3<br>Materialnedbrytning<br>12 veckor-1,7<br>24 veckor – 3,0<br>36 veckor – 3 +<br>Inflammatoriska parametrar (makrofager)<br>12 veckor – 3,0<br>24 veckor – 1,7<br>36 veckor – 1,7<br><u>Åtkomstställen femoral artär</u><br>Extern fibros<br>12 veckor – 1,3<br>24 veckor – 1,5<br>36 veckor – 1,7<br>Intern neointima<br>12 veckor – 3,7<br>24 veckor – 3,3<br>36 veckor – 3,8 |
|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                                                                             |      |            |                                                                                          |                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|-----------------------------------------------------------------------------|------|------------|------------------------------------------------------------------------------------------|---------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                             |      |            |                                                                                          |                                                               | Materialnedbrytning<br>12 veckor – 2,0<br>24 veckor – 3,0<br>36 veckor – 3+<br>Inflammatoriska parametrar (makrofager)<br>12 veckor – 3,5<br>24 veckor – 1,8<br>36 veckor – 1,8<br><br><u>Histomorfologiska värden för grad av öppenhet</u><br>Åtkomstställen karotis<br>12 veckor 74,0 %<br>24 veckor 81,9 %<br>36 veckor -89,43 %<br>Åtkomstställen femoral artär<br>12 veckor – 42,2 %<br>24 veckor – 73,21 %<br>36 veckor – 78,71 %<br><br><u>USA: grad av öppenhet i kärl (medelprocent)</u><br>Åtkomstställe karotis<br>12 veckor 94,6 %<br>24 veckor – 96,7 %<br>36 veckor – 94,7 %<br>Åtkomstställen femoral artär<br>12 veckor – 66,9 %<br>24 veckor – 63,6 %<br>36 veckor – 75,1 %<br><br>Slutsatser <ul style="list-style-type: none"> <li>Inga signifikanta tecken på lokal intolerans observerades (ingen synlig inflammatorisk, nekrotisk eller degenerativ lesion) vid 12, 24 eller 36 veckor</li> <li>Ingen signifikant ogynnsam vävnadsreaktion har registrerats vad gäller värd och enhet</li> <li>Nedbrytningen av implantatet var nästan fullständig efter 36 veckor</li> </ul> |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve | 2002 | Djurstudie | Syftet med studien var att utvärdera biokompatibiliteten och biofunktionaliteten hos ett | Implantationsperioden/uppföljningen är 5 veckor för alla djur | Eventuella tecken på biverkningar (inflammation, nekros, blödning eller annan                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |

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| Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France). | Radi Medical System AB<br><br>Utförs av Biomatech, Frankrike |  | biologiskt nedbrytbart implantat som utformats för att uppnå hemostas i kärlsystemet. Det testade instrumentet var avsett att föras in i punktionshål i artärer för att uppnå hemostas. En skiva fördes in i punktionshålet i artären och den andra drog åt den inre skivan från utsidan av artären. Båda skivorna fördes in genom en införrarhylsa. Skivorna utformades för att förhindra blödning, för att läka in i kärlväggen och slutligen brytas ned och absorberas. Studien utformades för att samla in och analysera data efter funktionell implantation hos får och gris för att utvärdera implantatets förmåga att upprätthålla den fysiologiska funktionen när det används i cirkulationssystemet, för att fastställa värdens respons och enhetens respons (fysisk integritet, vävnadsinkapsling vid avlivning) och för att utvärdera implantatets nedbrytning | 4 får, 1 gris<br><br>14 förslutningselement<br><br>8 förslutningselement implanterade i 2 får,<br><br>2 förslutningselement implanterade i 1 gris<br><br>När två förslutningselement implanterades i samma femorala artär implanterades de på ett avstånd > 30 mm | lesion) eller bildande av tunn pseudointimal vävnad registrerades. Särskild uppmärksamhet ägnades åt initial vävnadsintegration av enheten, med särskilt fokus på inkapslingen av den interna skivan.<br><br>Makroskopiskt observerades inga signifikanta tecken på lokal intolerans eller trombos. Den makroskopiska observationen visade ingen skillnad mellan fåret eller grisen efter implantation av förslutningselementen i de femorala artärerna. Makroskopiskt observerades inga signifikanta tecken på lokal intolerans eller trombos. Den makroskopiska observationen visade ingen skillnad mellan fåret eller grisen efter implantation av förslutningselementen i de femorala artärerna.<br><br>Den histopatologiska analysen av implantationsstället hos får visade inga lokala biverkningar. De inre och yttre skivorna uppvisade tecken på nedbrytning och hade i vissa fall brutits ned till mindre delar. De inre skivorna integrerades helt i neointimal vävnad. Hos grisen visade den histopatologiska analysen något fler inflammatoriska tecken runt de inre och yttre skivorna. På båda djuren uppvisade multifilamentet några fler |
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|                                                                                                                                                                                                              |                              |                                    |                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                | <p>tecken på inflammation än skivmaterialet, vilket är normalt för flätade suturer på grund av den större ytan.</p> <p>Kärlets öppenhet mättes efter 5 veckor med tre olika metoder: histomorfometri, histomorfometri i kombination med mätning av kärldiameter med hjälp av ett skjutmått, samt ultraljudsundersökning med färgdoppler. Den genomsnittliga graden av öppenhet i kärl hos får var mellan 60 och 80 % beroende på metod (12 observationer). Hos grisen var genomsnittlig grad av öppenhet i kärl mellan 40 och 80 % (2 observationer).</p> |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Första kliniska studien på människa</b>                                                                                                                                                                   |                              |                                    |                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Studiens namn                                                                                                                                                                                                | År/CI                        | Studiety                           | Syfte                                                                                                                                                                                                                                                                                                              | Milstolpar                                                                                                                                                                                                                                                                                                                                     | Potentiella acceptanskriterier                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Öppen, enarmad multicenterprövning | Syftet med studien var att fastställa säkerhet, prestanda och effektivitet för FemoSeal Vascular Closure System (FemoSeal System) i allmänhet, och specifikt förslutningselementen, hos patienter som genomgår hjärtdiagnostik eller interventionella kardiologiska ingrepp med åtkomst till den femorala artären. | <p>Tvådelad studie</p> <p>Totalt n = 80</p> <p>Del 1 n = 20</p> <p>Del 2 n = 60</p> <p>Indikationer</p> <p>Del 1 – Diagnostisk hjärkateterisering med femoral artär som åtkomstställe</p> <p>Del 2 – patienter som genomgår diagnostiska och interventionella hjärtingrepp med femoral artär som åtkomstställe</p> <p>30-dagarsuppföljning</p> | <p>Utfall</p> <p><u>-hemostas uppnådd med FS utan kompression</u></p> <p>- Del 1 20/20 (100 %)</p> <p>- Del 2 58/60 (97 %)</p> <p>Mediantid till hemostas vid tidpunkten för ingreppet (del 2) - 1,0 minuter (intervall omedelbart – 8 minuter)</p> <p><u>Tid till mobilisering (minuter)</u></p> <p>Del 1 –</p> <p>Medianvärde: 33,0</p> <p>medelvärde: 67,8</p> <p>Del 2 –</p> <p>medianvärde: 45</p>                                                                                                                                                   |



|  |  |  |  |  | <p>medelvärde: 87,5</p> <p><u>Incidens för stora kärlkomplikationer – uppföljning efter 30 dagar</u></p> <p>Del 1</p> <p>-Fri från vaskulära komplikationer 20/20 (100 %)</p> <p>Del 2</p> <p>Pseudoaneurysm – 1/59 (1,69 %)</p> <p><u>Behandlingsfel</u></p> <p>Del 1 – 0/20 (0 %)</p> <p>Del 2 – 3/60 (5 %)</p> <ul style="list-style-type: none"> <li>• 2 på grund av att hemostas inte kunde uppnås utan kompression</li> <li>• 1 på grund av större vaskulär komplikation, pseudoaneurysm</li> </ul> <p><u>Kontinuerlig utsöndring av sårvätska</u></p> <p>Del 1 – 0/20 (0 %)</p> <p>Del 2 – 8/60 (13 %)</p> <p><u>Hematom</u></p> <p>Del 1 – 0/20 (0 %)</p> <p>Del 2 – 6/60 (10 %)</p> |
|--|--|--|--|--|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Som en del av utvecklingsplanen före marknadsintroduktion för FemoSeal™ VCS genomfördes tre djurtester. Innan kliniska studier inleddes år 2000 genomfördes en djurstudie för att utvärdera den biologiska funktionaliteten hos FemoSeal™ VCS. I denna studie utvärderades förslutningselementens förmåga att upprätthålla den fysiologiska funktionen och förslutningselementens nedbrytning. Vid 18 månader var det inre och yttre skivmaterialet inte längre synligt efter att ha ersatts med en endoluminal fibrös vävnad. Sammanfattningsvis bekräftades kapaciteten hos FemoSeal™ VCS förslutningselement för att upprätthålla fysiologisk funktion när det används i det cirkulatoriska systemet.

2002 genomfördes en djurstudie för att utvärdera biokompatibiliteten och biofunktionaliteten hos ett biologiskt nedbrytbart implantat, FemoSeal™ VCS, utformat för att uppnå hemostas i kärlsystemet. Sammanfattningsvis var nedbrytningen av implantatet nästan fullständig efter 36 veckor och det förekom ingen signifikant ogynnsam vävnadsreaktion.

En annan djurstudie år 2002 utvärderade biokompatibiliteten och biofunktionaliteten hos ett biologiskt nedbrytbart implantat, FemoSeal™ VCS, utformat för att uppnå hemostas i kärlsystemet. Efter 5 veckor var inkapslingen av skivan komplett och tecken på nedbrytning observerades för inre och yttre skivor. Sammanfattningsvis bekräftades implantatets förmåga att upprätthålla fysiologisk funktion när det användes i det cirkulatoriska systemet.

Som en del av den kliniska utvecklingsplanen för FemoSeal™ VCS genomförde Radi Medical System AB en klinisk prövning före marknadsintroduktion. Denna kliniska prövning är inte publicerad eller tillgänglig online. Studien med enhetsmodell #11200 utfördes 2002-2004 enligt den europeiska standarden EN 540 (Clinical Investigation of Medical Devices for Human Subjects) och i enlighet med ICH General Considerations for Clinical Trials and Guideline for Good Clinical Practice. Detaljerna i denna studie dokumenteras i rapporten EU-SE-001. Den kliniska prövningen har dokumenterats i slutrapporten från Radi Medical Systems AB – ”Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures”. Den kliniska studien utfördes med FemoSeals™ första modell #11200 och fokuserade på säkerheten och effektiviteten hos de implanterbara förslutningskomponenterna. Den enda skillnaden mellan den första modellen #11200 och den nuvarande modellen, C11202, är storleken, 6F respektive 7F, och det förbättrade leveranssystemet. De kliniska fördelarna, den avsedda användningen, användningsprinciperna och råmaterialen i de implanterbara förslutningselementen, den inre förseglingen och den yttre låsskivan kvarstår oförändrade.

Enhetens avsedda användning var för patienter som genomgick diagnostiska hjärt- eller interventionella hjärtingrepp med den femorala artären som åtkomstpunkt. Syftet med denna studie var att fastställa säkerhet, prestanda och effektivitet hos FemoSeal™ VCS. Detta var en prospektiv, enarmad och öppen multicenterstudie med 30 dagars uppföljning.

Den primära funktionsslutpunkten var tid till hemostas, definierat som frånvaro av rikliga blödningar. Den primära säkerhetsslutpunkten var incidensen av allvarliga kärlkomplikationer under 30 dagar. Sekundära slutpunkter var tid till mobilisering, andelen behandlingsmisslyckanden, incidens av biverkningar och produktens prestandaegenskaper under leverans och driftsättning.

Patienterna i denna studie var vuxna som kunde ge informerat samtycke och med minst en pedalpuls. Patienter uteslöts från studien om de hade något av följande tillstånd:

- Anamnes på perifer kärlsjukdom

- Autoimmuna sjukdomar
- Känd blödningssjukdom vid svår anemi
- INR >1.5
- Hjärtinfarkt inom 72 timmar
- Okontrollerad hypertoni trots behandling
- Fetma som förhindrar åtkomst med Seldinger-teknik
- Förekomst av kärltransplantat eller stent vid arteriotomistället
- Tidigare ipsilateral punktion inom 3 månader
- Förväntad livslängd < 6 månader

Dessutom undersöktes patienterna intraoperativt och exkluderades från studien om något av följande observerades:

- Lumendiameter för femoral artär <5 mm
- Artärgrenar inom 2 cm från punktionsstället
- Signifikant stenosis inom 3 cm från punktionsstället
- Användning av den primära införlshylsan >6Fr
- Punktion vid eller distalt om den femoral artärens bifurkation
- Flera femoralpunktioner
- Känd eller misstänkt punktion av den bakre femoralväggen
- Stort hematoma (2:6 cm) när ingreppet är slutfört
- Svårt att föra in den primära hylsan vid ingrepp på grund av slingrig vävnad eller slingriga kärl

Denna studie med ett protokoll genomfördes i två delar: 20 patienter rekryterades till del 1 varefter en säkerhetsanalys genomfördes och sedan rekryterades ytterligare 60 patienter till del 2.

I del 1 var genomsnittsåldern för de rekryterade patienterna 65,9 år, 70,0 % av patienterna var män och 95 % av patienterna stod på samtidig medicinering. I del 2 av studien var genomsnittsåldern 63,8 år, 78 % var män och 100 % stod på samtidig medicinering.

Patienter som genomgick diagnostiska (del 1 och del 2) eller interventionella (del 2) hjärkateteriseringsprocedurer kunde rekryteras till studien. Procedurerna överensstämde med vårdstandarden på vart och ett av de inskrivna sjukhusen, följt av användning av FemoSeal™ VCS. Patientdata samlades in vid startpunkten, under proceduren och 1 dag och 30 dagar efter

proceduren. Resultaten sammanfattas i **tabell 1.5** och indikerar att FemoSeal™ VCS är säker och effektiv att använda i denna patientpopulation.

**Tabell 1.5 Kliniska resultat rapporterade i förmarknadsstudien**

|                                                                                                                | Del 1        | Del 2                     |
|----------------------------------------------------------------------------------------------------------------|--------------|---------------------------|
| Antal patienter                                                                                                | 20           | 60                        |
| Genomsnittlig tid till hemostas                                                                                | 1,2 minuter  | 1,6 minuter <sup>a</sup>  |
| Genomsnittlig tid till ambulation                                                                              | 72,2 minuter | 87,5 minuter <sup>b</sup> |
| Incidens av större vaskulära komplikationer <sup>c</sup>                                                       | 0 (0 %)      | 1 (2 %)                   |
| Antal patienter med biverkningar                                                                               | 5 (25 %)     | 19 (32 %)                 |
| Behandlingssvikt (definieras som större vaskulära komplikationer, behov av manuell kompression eller bådadera) | 0 (0 %)      | 3 (5 %)                   |
| Funktionsfel                                                                                                   | 0 (0 %)      | 6 (10 %)                  |

<sup>a</sup> Baserat på en total provstorlek på 58 eftersom 2 patienter inte uppnådde hemostas vid tidpunkten för ingreppet på grund av tidigare ipsilaterala punktioner. Hemostas uppnåddes efter 7 minuter och 37 minuter för dessa patienter.

<sup>b</sup> Baserat på en total provstorlek på 59: 1 patient inkluderades inte eftersom patienten var placerad på ventilator på grund av lungödem och inte kunde röra sig på över en vecka.

<sup>c</sup> Definition av vaskulär komplikation som kräver blodtransfusion eller kirurgisk reparation, eller lokal infektion som kräver administrering av antibiotika, sjukhusinläggning eller förlängning av sjukhusvistelsen, eller debridering av platsen

Inga större vaskulära komplikationer observerades i del 1 av studien. En (1) större vaskulär komplikation rapporterades i del 2 av studien: pseudoaneurysm som rapporterades inom en dag efter ingreppet. Händelsen krävde ultraljudsvägledd kompression och en injektion av trombin i pseudoaneurysmet och förlängde patientens sjukhusvistelse.

Av de fem biverkningar som rapporterades i del 1 av studien fanns det en (1) möjlig enhetsrelaterad biverkning: en icke-allvarlig händelse med rikliga blödningar 1 dag efter ingreppet. Av de 19 biverkningar som rapporterades i del 2 av studien observerades tre produktrelaterade icke-allvarliga biverkningar av hematom, och sex eventuellt enhetsrelaterade

icke-allvarliga händelser observerades, inklusive tre rapporter om kvarstående utsöndring av sårvätska, två om hematom och en (1) om bensmärta efter träning.

Behandlingen anses som misslyckad för tre patienter i del 2: Två på grund av att hemostas inte uppnåddes utan användning av kompression och en (1) på grund av den allvarliga vaskulära komplikationen (pseudoaneurysm). Inga behandlingsmisslyckanden inträffade i del 1 av studien.

Av de sex enhetsfunktionsfelen i del 2 av studien var det tre som inte störde proceduren, ett tillskrevs handhavandefel, ett var läckage i införaren och en var en trasig filamentled. De resterande två felen åtgärdades i med modelluppdateringar som implementerades i C11202.

Del 2 av den kliniska studien före marknadsintroduktionen rapporterade inte uppföljningsresultaten efter 6 månader på grund av att patienter inte följde ordinationen. 30-dagarsresultaten från den kliniska studien före marknadsintroduktionen (EU-SE-001), som är i linje med den kliniska litteraturens uppföljningsperiod, visar att FemoSeal™ VCS är säker och effektiv.

#### 1.4.2 Sammanfattning av data från kliniska studier efter marknadsintroduktion

Det fanns fyra slutförda kliniska studier efter marknadsintroduktion som beskrivs i **tabell 1.6** nedan. Dessa kliniska undersökningar publiceras inte och är inte tillgängliga online.

**Tabell 1.6 Kliniska studier efter marknadsintroduktion**

| Slutförda kliniska studier efter marknadsintroduktion                                       |                             |                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                    |                                                                                                                                    |
|---------------------------------------------------------------------------------------------|-----------------------------|-----------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|
| Studiens namn                                                                               | År/CI                       | Studietyp                                                 | Syfte                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Milstolpar                                                                                                                                                                                                                                                                                                         | Potentiella acceptanskriterier                                                                                                     |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI                | Eftermarknadsstudie, användaracceptans för ny förpackning | Eftermarknadsstudie utförd på FemoSeal Vascular® Closure System #11202, som har ett modifierat leveranssystem jämfört med den första modellen #11200, för att dokumentera funktionaliteten.<br><br>Syftet med studien var att få återkoppling på den reviderade bruksanvisningen, utbildningsprojektet för läkare och sjuksköterskor, för att bekräfta de bedömningar som gjorts i riskanalysen och för att ge input till eventuella förbättringar av produktkvaliteten. | 100 patienter <ul style="list-style-type: none"> <li>63 män/37 kvinnor</li> <li>Medelålder 68 år för kvinnor, 65 år för män</li> </ul> 2 svenska sjukhus, 6 läkare<br><br>112 enheter<br><br>Data som samlats in i patientjournalformulär<br><br>Planerad observationstid – 30 minuter från appliceringstillfället | Utfall<br><br>1. Bilder/instruktioner i bruksanvisningen anses vara informativa och adekvata<br><br>2. Omedelbar hemostas (91/100) |
| Confirmatory Assessment of FemoSeal™ Vascular                                               | Dr Nicolas Moes<br>Innsbruk | Bekräftande bedömning efter                               | Syftet med denna studie var att bedöma säkerhet och prestanda för FemoSeal®                                                                                                                                                                                                                                                                                                                                                                                              | 50 patienter i följd                                                                                                                                                                                                                                                                                               | Primära slutpunkter <ul style="list-style-type: none"> <li>Primär effektivitetsslutpunkt –</li> </ul>                              |

|                                                                                |                               |                      |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
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| Closure System in 7F-Sheath. (2008)                                            | Medical University, Österrike | marknadsintroduktion | som används under normala kliniska rutiner hos patienter som genomgår diagnostisk hjärtkateterisering eller perkutan interventionell hjärtprocedur som utförs med 7F-hylsa.                                                                                                                   | Indikation – diagnostisk eller invasiv hjärtkateterisering från en gemensam femoral artär <table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                                                                                                                                                                                                                                      | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | TTH (tid till hemostas) med eller utan utsöndring av sårvätska men utan ytterligare kompression, manuell eller mekanisk. <ul style="list-style-type: none"><li>Säkerhetsslutpunkter – incidens av biverkningar – mindre och större vaskulära komplikationer och alla andra biverkningar – allvarliga och icke allvarliga under studiens varaktighet (dvs. fram till utskrivning av patienten).</li></ul> Utfall <ul style="list-style-type: none"><li>Genomsnittlig tid till hemostas</li><li>Diagnostik – 56,6 ± 29 sekunder</li><li>Ingrepp 59,9 ± 16,2 sekunder</li><li>Alla patienter 57,8 ±26,3</li><li>Alla patienter kunde förflyttas utan problem efter 4 timmars sängvila.</li></ul> Säkerhetsresultat <ul style="list-style-type: none"><li>49/50 (98 %) utan vaskulära komplikationer fram till utskrivning från sjukhuset</li><li>Genomsnittlig tid till utskrivning 2,6 dagar</li><li>1/50 (2 %) mindre blödning nästa dag efter händelselös promenad på angiografidagen</li></ul> |
| n                                                                              | 50                            |                      |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| men                                                                            | 35 (70%)                      |                      |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| women                                                                          | 15 (30%)                      |                      |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| PCI cases                                                                      | 15                            |                      |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| age (yrs)                                                                      | 62.8±11.1                     |                      |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| body mass index (kg/m²)                                                        | 25.4±6.7                      |                      |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| systolic BP (mmHg)                                                             | 131.2±20.9                    |                      |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| diastolic BP (mmHg)                                                            | 77.9±10.6                     |                      |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| diabetes mellitus                                                              | 9 (18%)                       |                      |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| arterial hypertension                                                          | 34 (68%)                      |                      |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| previous coronary intervention                                                 | 13 (26%)                      |                      |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| preprocedure aspirin                                                           | 50 (100%)                     |                      |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| preprocedure clopidogrel                                                       | 50 (100%)                     |                      |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Procedural unfractionated heparin                                              | 15 (30%)                      |                      |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Procedural abciximab                                                           | 2 (4%)                        |                      |                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                        |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009) | 2009 RADI                     | Eftermarknadsstudie  | Studien ska undersöka huruvida kunderna/användarna upplevde några problem med den nya förpackningen, särskilt den icke-sterila utsidan av Tuvek/PET-PE-påsen.<br><br>Studien ska också undersöka om den behandlande läkaren uppfattar några skillnader i stegen för applicering/insättning av | 25 enheter<br><br>4 svenska sjukhus<br><br>16/25 (64 %) av patienterna var PCI-patienter med tunga antikoagulantia                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Utfall<br><br>1. Förpackningsrelaterade problem – 21/25 (84 %) appliceringar lyckades; 4/25 (16 %) misslyckades (1 – test av ny införare, 1 inre skiva gick igenom arteriotomin vid backningssteget, knappen sköts upp och den yttre skivan placerades i vävnadskanalen i snittet, och i 2 fall uppnåddes inte direkt hemostas trots lyckad införing). |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |

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|----------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|--------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                        |                                        |                                                              | <p>enheten jämfört med tidigare använda enheter.</p> <p>Studien bör också tillhandahålla input för eventuella ytterligare behov av förbättring av produktkvaliteten.</p>                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                | <p>2. Omedelbar hemostas 19/25 (76 %) patienter</p> <p>3. Blödning 11/25 (44 %) - 9/25 (36 %) utsöndring av sårvätska/blödning, 2/25 (8 %) hematoma</p> <p>Total händelsefrekvens 19 %</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <p>The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022)</p> | <p>2022/Terumo Medical Corporation</p> | <p>Prospective, Multi-center, Observational, Post-market</p> | <p>För att ytterligare demonstrera säkerheten och effektiviteten hos FemoSeal™ VCS när det gäller att uppnå hemostas vid åtkomstställen i den femorala artären (CFA) hos verkliga patienter som genomgår perkutana endovaskulära ingrepp</p> | <ul style="list-style-type: none"> <li>• Patientuppföljning vid 30 dagar (<math>\pm 7</math> dagar) genom sjukhusbesök eller telefonsamtal.</li> <li>• Registrering: december 2021 till juli 2022.</li> <li>• 230 rekryterade patienter som genomgår diagnostiska eller interventionella endovaskulära procedurer där FemoSeal™ används.</li> </ul> <p>Tre europeiska platser: Frankrike (92 patienter), Tyskland (38 patienter), Belgien (100 patienter).</p> | <ul style="list-style-type: none"> <li>• <b>Demografi/komorbiditeter:</b> <ul style="list-style-type: none"> <li>- Kön: 161 män (70 %)/69 kvinnor (30 %).</li> <li>- Medelålder: <math>70 \pm 12</math>.</li> <li>- BMI: <math>26,1 \pm 4,95</math> kg/m<sup>2</sup>.</li> <li>- Hypertoni: 160 patienter (69,6 %).</li> <li>- Dyslipidemi: 128 (55,7 %).</li> <li>- Kranskärslssjukdom: 42 (18,3 %).</li> <li>- Nuvarande rökare: 86 (37,6 %).</li> <li>- Tidigare rökare: 66 (28,8 %).</li> <li>- Kranskärslssjukdom: 34 (14 %).</li> <li>- Föregående myokardinfarkt: 18 (7,8 %).</li> <li>- Revaskularisering av perifer artär: 12 (5,2 %) karotis och 83 (37,5 %) artär i nedre extremitet.</li> <li>- Trombocythämmande behandling (vid baslinjen): 211 (91,7 %), inklusive 21 (9,1 %) med dubbel trombocythämmande behandling (DAPT).</li> <li>- Antikoagulering oralt: 40 (17,4 %) patienter.</li> </ul> </li> <li>• <b>Interventionsegenskaper:</b> <ul style="list-style-type: none"> <li>- Miljö: slutenvårdsklinik 162 fall (70,4 %), öppenvårdsklinik 68 fall (29,6 %).</li> <li>- Rådande indikation: claudicatio 147 fall (63,9 %).</li> </ul> </li> </ul> |

|  |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|--|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <ul style="list-style-type: none"> <li>- Förfaringssätt: 35 antegrad (15,3 %), 194 retrograd (84,7 %).</li> <li>• <b>Primära slutpunkter:</b> <ul style="list-style-type: none"> <li>- Kombinerad slutpunkt för säkerhet (fritt från allvarliga komplikationer vid åtkomststället inom sex timmar efter ingreppet) och effektivitet (framgångsrik hemostas vid punktionsstället) uppnåddes hos 215/226 (95,1 %) [95 % KI: 91,46; 97,55] patienter i den fullständiga analysen och hos 215/230 (93,5 %) [95 % KI 89,47, 96,30] patienter i FemoSeal™-behandlingsgruppen.</li> <li>- Slutpunkten för effektivitet uppnåddes hos 219/226 (96,9 %) KI [93,7, 98,7] patienter.</li> <li>- Slutpunkten för effektivitet uppnåddes hos 220/230 (95,2 %) [95 % KI: 92,15, 97,90] patienter.</li> </ul> </li> <li>• <b>Sekundära slutpunkter:</b> <ul style="list-style-type: none"> <li>- Fritt från mindre komplikationer vid åtkomststället sex timmar efter ingreppet, uppnåddes hos 225/230 (97,8 %) [95 % KI: 95,00; 99,29] patienter.</li> <li>- Fritt från större och mindre komplikationer vid åtkomststället från sex timmar till 30 dagar efter ingreppet, uppnåddes hos 219/230 (95,2 %) [95 % KI: 91,60; 97,59] patienter.</li> <li>- Mediantid till hemostas med FemoSeal™ VCD: 0,42 (0,25; 0,50) minuter.</li> <li>- Genomsnittlig tid till ambulation: 5,00 (4,54; 5,50) minuter.</li> </ul> </li> </ul> |
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|--|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  |  |  |  |  | <p>- Genomsnittlig längd på sjukhusvistelse: 23,98 (22,72, 25) timmar.</p> <p>- Användbarhet för FemoSeal™ VCS: "lätt" eller "mycket lätt" att föra in i 98,7 % av fallen ("lätt" att föra in i 21 (9,2 %), "mycket lätt" att föra in i 205 (89,5 %)) med inget eller lågt motstånd vid utplacering i 226 (98,3 %) av fallen.</p> <p>152/230 (66,1 %) av patienterna behandlades med ledare som ingår i FemoSeal™-satsen (GW 0,038") och rekommenderas i FemoSeal™ utan några rapporterade produktbrister eller biverkningar.</p> |
|--|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Studien 2006 genomfördes för att bekräfta säkerheten och effektiviteten hos den nuvarande enheten med ett förbättrat leveranssystem och för att få återkoppling på bruksanvisningen och utbildningsprogrammet för FemoSeal™ VCS. Studien omfattade 100 patienter och den primära slutpunkten var att undersöka om hemostas uppnåddes eller om ytterligare manuella eller mekaniska kompressioner behövdes. I denna studie drogs slutsatsen att användningen av FemoSeal™ VCS var framgångsrik i majoriteten av fallen (91 % uppnådde omedelbar hemostas).

I 2008 års studie deltog 50 patienter för att bedöma säkerhet och prestanda hos FemoSeal™ VCS vid användning under normala kliniska rutiner hos patienter som genomgick hjärkateterisering med en 7F-hylsa. Studiens primära slutpunkt var att samla in data om tiden till hemostas och tiden till mobilisering utan ytterligare kompression, manuell eller mekanisk. I studieresultaten drogs slutsatsen att den genomsnittliga tiden till hemostas var 57,8 sekunder och att alla patienter kunde vara uppe och röra på sig efter 4 timmars sängliggande.

Studien från 2009 utfördes i syfte att utvärdera den nya FemoSeal™ VCS-förpackningen. 25 patienter rekryterades till studien. Den primära slutpunkten var om användaren upplevde några problem med förpackningen. Användarna noterade inga problem med den nya FemoSeal™ VCS-förpackningen. Denna studie samlade också in data om tiden till hemostas.

Syftet med studien från 2022 var att proaktivt samla in data om säkerheten och effektiviteten hos FemoSeal VCS när det gäller att uppnå hemostas vid åtkomstställen i den femorala artären (CFA) hos verkliga patienter som genomgår perkutana endovaskulära ingrepp. 230 patienter

rekryterades till studien. De primära slutpunkterna för studien är lyckat förfarande (dvs. lyckad hemostas vid punktionsstället) och minskning av allvarliga komplikationer (t.ex. kärlskada, blödning vid åtkomststället, infektion vid åtkomststället, upprepad manuell kompression och ny ipsilateral akut benischemi vid åtkomststället). Studien kom fram till att FemoSeal™ VCS fungerar bra i verkliga miljöer och ger effektiv hemostas och låga frekvenser av komplikationer vid åtkomststället för patienter som genomgår perifera endovaskulära ingrepp. Den uppvisar god prestanda med kort tid till hemostas och god användarvänlighet, vilket gör FemoSeal™ VCS till en värdefull enhet för förslutning av femoral åtkomst.

### 1.4.3 Sammanfattning av data från kliniska studier efter marknadsintroduktion

#### 1.4.3.1 Slutförda uppföljande kliniska undersökningar efter marknadsintroduktion

En sammanfattning av de slutförda kliniska uppföljningsaktiviteterna efter marknadsintroduktionen beskrivs i **tabell 1.7** nedan.

**Tabell 1.7. Kliniska uppföljningsaktiviteter efter marknadsintroduktion**

| Slutförda kliniska uppföljningsaktiviteter efter marknadsintroduktion     |          |                                                                              |                                                                                                                                                                                       |                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|---------------------------------------------------------------------------|----------|------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Aktivitetsnamn                                                            | År/CI    | Studietyp                                                                    | Syfte                                                                                                                                                                                 | Milstolpar                                                                                                                                  | Potentiella acceptanskriterier                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021 TMC | Klinisk undersökning efter marknadsintroduktion – högkvalitativ undersökning | Undersökning efter marknadsintroduktion för att samla in prospektiv återkoppling relaterad till användningen av FemoSeal™ Vascular Closure Device som distribueras på EU-marknaderna. | <ul style="list-style-type: none"> <li>120 fall</li> <li>8 unika läkare med &gt; 5 års erfarenhet</li> <li>Flera länder i Europa</li> </ul> | <p><b>Enhetsutvärderingar på en 1–5-skala – undersökningsutlåtanden</b></p> <ul style="list-style-type: none"> <li>Kriterier för godkännande <ul style="list-style-type: none"> <li>Betyg 3–5 bedöms som fördelaktiga</li> <li>Alla utlåtanden ska ha ≥ 80 % positiv feedback</li> </ul> </li> <li>Utfall <ul style="list-style-type: none"> <li>Inget undersökning samlat in har mottagits &gt; 20 % ogynnsamma svar</li> <li>Inga klagomål mot</li> </ul> </li> </ul> |

| Slutförda kliniska uppföljningsaktiviteter efter marknadsintroduktion                                                           |                  |                                                                              |                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|---------------------------------------------------------------------------------------------------------------------------------|------------------|------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                 |                  |                                                                              |                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                         | produkten har angivits                                                                                                                                                                                                                                                                                                                                                                                                                               |
| 20210298 – 0,035” and 0038” Guidewire Clinical Survey Report (2021)                                                             | 2021 TMC         | Klinisk undersökning efter marknadsintroduktion – högkvalitativ undersökning | Undersökning efter marknadsintroduktion för att samla in prospektiv feedback relaterad till användningen av 0,035”-ledaren som ingår i 6 Fr Angio-Seal™ VIP Vascular Closure Device (VCD) och 0,038”-ledaren som ingår i både 8 Fr Angio-Seal™ VIP VCD och FemoSeal Vascular Closure System som distribueras på EU-marknaderna. | <ul style="list-style-type: none"> <li>Undersökningar för 0,035”-ledare <ul style="list-style-type: none"> <li>106 undersökningar</li> <li>64 läkare</li> </ul> </li> <li>Undersökningar för 0,038”-ledare <ul style="list-style-type: none"> <li>109 undersökningar</li> <li>55 läkare</li> </ul> </li> <li>12 retrospektiva undersökningar</li> </ul> | <b>Enhetsutvärderingar på en 1–5-skala – undersökningsutlåtanden</b> <ul style="list-style-type: none"> <li>Kriterier för godkännande <ul style="list-style-type: none"> <li>Betyg 3–5 bedöms som fördelaktiga</li> <li>Alla utlåtanden ska ha ≥ 80 % positiv feedback</li> </ul> </li> <li>Utfall <ul style="list-style-type: none"> <li>Alla ledare fick godtagbara betyg</li> <li>Inga klagomål mot produkten har angivits</li> </ul> </li> </ul> |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024 TMC/TE | Klinisk undersökning efter marknadsintroduktion – högkvalitativ undersökning | Att prospektivt samla in feedback relaterad till användningen av FemoSeal VCS med ledare som distribueras på EU-marknaden.                                                                                                                                                                                                      | <ul style="list-style-type: none"> <li>126 undersökningar</li> <li>7 platser</li> <li>5 länder</li> <li>14 november 2023-11 juni 2024</li> <li>Läkarens specialitet: <ul style="list-style-type: none"> <li>Kärlkirurg</li> </ul> </li> <li>Interventionell radiologi</li> <li>Angiologi</li> </ul>                                                     | <b>5 Enhetsutvärderingar – undersökningsutlåtanden</b> <ul style="list-style-type: none"> <li>Kriterier för godkännande <ul style="list-style-type: none"> <li>Betyg 3–5 bedöms som fördelaktiga</li> <li>Alla utlåtanden ska ha ≥ 80 % positiv feedback</li> </ul> </li> <li>Om oönskade händelser inträffar i denna undersökning bör de vara förutsedda av riskhanteringen.</li> <li>Patientdemografi</li> </ul>                                   |

| Slutförda kliniska uppföljningsaktiviteter efter marknadsintroduktion |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-----------------------------------------------------------------------|--|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                       |  |  |  |  | <ul style="list-style-type: none"> <li>○ Kvinna: 29,4 % (37/126)</li> <li>○ Man: 69,8 % (88/126)</li> <li>○ Kön ej uppgett: 0,8 (1/126)</li> <li>○ Ålder &gt;75 år: 31,7 %</li> <li>• Utfall <ul style="list-style-type: none"> <li>○ Ledare som medföljer FemoSeal™ VCS: 101/126 (80,2 %).</li> <li>○ Varaktighet för procedur (minuter): 63,4 (36,6) (medelvärde (SD)); 57,0 (36,0-81,0) (median (IQR))</li> <li>○ Alla prestandabetyg för FemoSeal™ VCS var gynnsamma.</li> <li>○ Alla betyg för FemoSeal™ VCS-ledare var gynnsamma.</li> <li>○ En biverkning (0,8 %): FemoSeal™ VCS-skivorna var inte korrekt inriktade, troligen på grund av användning av en styv ledare (Boston</li> </ul> </li> </ul> |

| Slutförda kliniska uppföljningsaktiviteter efter marknadsintroduktion |  |  |  |  |                                                                                                                                     |
|-----------------------------------------------------------------------|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------|
|                                                                       |  |  |  |  | Scientific<br>Amplatz<br>Super Stiff,<br>75 cm, 0,035<br>tum) som<br>krävde<br>manuell<br>kompression<br>för att uppnå<br>hemostas. |

Terumo Medical Corporation har genomfört tre högkvalitativa användarundersökningar för läkare under den aktuella rapporteringsperioden (1 september 2019-31 augusti 2024).

FemoSeal™ Clinical Surveys samlade in proaktiva kliniska data i relation till säkerheten och prestandan hos FemoSeal™ VCS under klinisk användning. Undersökningen omfattade frågor som fokuserade på den övergripande enheten och associerade tillbehör, inklusive 0,038”-ledaren och direkta interaktioner mellan enheten och tillbehören. De kliniska undersökningarna om ledare samlade in proaktiva kliniska data avseende säkerhet och prestanda vid klinisk användning av 0,038”-ledaren som levererades med FemoSeal™ VCS. Frågorna i undersökningen fokuserade specifikt på den allmänna användningen av ledaren, från införande genom ingreppshylsan in i vaskulaturen till avlägsnande av ledaren.

FemoSeal™ VCS och 0,038”-ledaren som medföljer enheten klassificerades som godkänd av alla undersökningsdeltagare, sex (6) klagomål om enheten lämnades in, och nio (9) icke-klagomål om ledaren lämnades in baserat på en utvärdering av de kommentarer som erhöles från de högkvalitativa kliniska undersökningarna. Klagomålen har utvärderats för både FemoSeal och ledaren och bedömdes som en del av Terumos övervakningsprocess efter godkännandet för försäljning. Inga nya risker och/eller risknivåer identifierades.

En användarundersökning för läkare genomfördes 2024 som en del av aktiviteterna för klinisk uppföljning efter marknadsintroduktion (PMCF). Resultaten av undersökningen visade att betygen för prestanda och säkerhet för FemoSeal™ VCS överlag var mycket gynnsamma. Kompatibiliteten hos andra ledare än den standardversion som medföljer FemoSeal™ VCS visades också.

**1.4.3.2 Pågående/planerad klinisk uppföljning efter marknadsintroduktion**

TMC har en pågående/planerade kliniska uppföljningsaktiviteter efter marknadsintroduktion. En klinisk undersökning kommer att genomföras för att prospektivt samla in feedback om användningen av ledaren med FemoSeal VCS som distribueras på EU-marknaden. Undersökningen kommer att fyllas i av läkare för att studera vilka ledare de använde under

proceduren. Syftet med denna undersökning är att åtgärda en lucka som identifierats som bristen på litteratur och kommentarer från externa granskare om kompatibiliteten för FemoSeal™ VCS med andra ledare från andra varumärken än Terumo. Återkopplingen omfattar tekniska resultat, klinisk prestanda och säkerhet som rör enhetens prestanda med olika ledare.

#### 1.4.4 Sammanfattning av data från systematisk litteraturgranskning

Terumo Medical Corporation genomför systematiska litteraturgranskningar för att samla in och utvärdera kliniska säkerhets- och prestandadata från publicerade studier av FemoSeal™ VCS och/eller liknande produkter. Syftet med den årliga granskningen av den publicerade litteraturen är att identifiera tidigare okända biverkningar, övervaka kända biverkningar, identifiera framväxande risker och identifiera möjlig systematisk felaktig användning eller off-labelanvändning av FemoSeal™ VCS.

Den senaste systematiska litteraturgranskningen, som omfattade perioden 1 september 2019 till 31 augusti 2024, identifierade 29 publicerade studier som gav kliniska säkerhets- och prestandadata för FemoSeal™ VCS. Tjugotre referenser rapporterade användning av FemoSeal™ VCS på etiketten och off label-användning rapporterades i nio studier. Sammantaget visar litteraturgranskningen av specifika studier för användning av FemoSeal™ VCS en studiepopulation som är representativ för patienter i EU som genomgår perkutan kärllkateterisering. Se **avsnitt 3** för en lista över dessa 23 fackgranskade publikationer.

Klinisk prestanda bedömdes med följande mått:

- Tiden till hemostas är bättre än eller jämförbar med den senaste tekniken för perkutan förslutning av femoralartärpunktion.
- Tiden till mobilisering är bättre än eller jämförbar med den senaste tekniken för perkutan förslutning av den gemensamma femoralartären.
- Frekvensen av postoperativa komplikationer är jämförbar eller lägre än nuvarande standardvård.

Baserat på dessa kliniska prestandamått visade data i denna litteraturgenomgång att FemoSeal™ VCS kan användas med framgång för att försluta den femorala arteriella punktionen (arteriotomi) hos patienter som har genomgått perkutan kateterisering med en 7 Fr-hylsa eller mindre ingreppshylsa. Fullständig hemostas uppnåddes hos majoriteten av patienterna (79,65-100 %) och var förknippad med en mediantid till hemostas på 0,5 min och medeltid till utskrivning på 3 dagar. Mellan 69,2 och 86,7 % av patienterna kunde röra sig 5 timmar efter förslutning, med en genomsnittlig postoperativ bästa tid på 349 minuter. Fel på FemoSeal™ VCS observerades i 3,68-4 % av fallen och ytterligare manuell kompression krävdes i 0,9-4,4 % av ingreppen.

Klinisk säkerhet bedömdes med hjälp av biverkningar, inklusive men inte begränsat till:

- Blödning
- Hematom
- Pseudoaneurysm
- Blåmärken
- Arteriovenös fistel
- Infektion
- Dödsfall

För var och en av dessa biverkningar var frekvensen som rapporterades för FemoSeal™ VCS i de inkluderade studierna lägre än eller jämförbar med historiskt rapporterade frekvenser för manuell kompression och andra kärlförslutningsenheter.

Inga biverkningar identifierades genom granskning av 10 fallrapporter, eftersom inga nya, oförutsedda, framväxande eller oacceptabla risker identifierades.

Den övergripande effektiviteten vid användning av FemoSeal™ VCS under diagnostisk angiografi eller interventionella operationer beror på flera faktorer som: kön, ålder, patientens anatomi, komorbiditeter, anatomisk placering av punktionsstället, kirurgens erfarenhet, metod för placering av VCD, postoperativ vård, osv. Förutom teknisk framgång, inklusive uppnådd hemostas, erbjöd FemoSeal™ VCS klinisk nytta jämfört med kärlförslutning efter punktering av femoralartären, såsom kortare tid till hemostas och kortare tid till mobilisering.

Prestandaresultaten för FemoSeal™ VCS överensstämmer med de som förväntas för denna typ av enhet när den används såsom avsett. Några av de referenser som hämtades under den aktuella sökperioden visade användning av den undersökta enheten på en annan anatomisk plats än den gemensamma femoralartären och för förslutning av arteriotomier > 7 Fr, vilket anses vara off-label.

Inga okända biverkningar, framväxande risker eller möjlig systematisk felaktig användning av enheten identifierades under granskningen. Men om FemoSeal™ VCS används med försiktighet av utbildade läkare fungerar den medicintekniska produkten som en användbar och nödvändig klinisk produkt. Sammantaget tillgodoser målbehandlingen och därmed FemoSeal™ VCS det kliniska behov som för närvarande finns vid behandling av komplikationer relaterade till vaskulär åtkomst.

Sammantaget visade data från denna litteraturgranskning inte på några prestanda- eller säkerhetsproblem i den kliniska miljön som tidigare inte var kända, eller negativa effekter som uppträdde med högre än förväntad/acceptabel frekvens. Av denna litteraturöversikt kan man därför dra slutsatsen att FemoSeal™ VCS fortsätter att fungera som förväntat när den används för att ge kompression för hemostas vid arteriotomin efter perkutan kateterisering och inte är förknippad med allvarliga säkerhetsrisker.

#### 1.4.5 Sammanfattning av data från övervakning efter marknadsintroduktion

Ett proaktivt PMS-system finns på plats och en genomgång av alla klagomål görs månatligen och i enlighet med interna tillverkningsrutiner. Reklamationsdata analyserades under tidsperioden 1 september 2019 till 31 augusti 2024. Totalt inkom 28 MDV-rapporter (Medical Device Vigilance) och 476 kundklagomålsrapporter till tillverkaren. Av de 28 MDV-rapporterna var 27 relaterade till biverkningar och en till funktionsfel på enheten. Det förekom två dödsfall under rapporteringsperioden, men inget av de rapporterade dödsfallen bedömdes vara relaterat till studieprodukten. Av de 476 klagomål som lämnades in till tillverkaren var de vanligaste orsakerna till klagomålen svårigheter vid införandet (146 förekomster, 0,0142 % förekomstfrekvens). Felläge för utdragningshändelser är det näst vanligaste med en frekvens på 0,0126 % (130 händelser).

Fler än 1 030 136 FemoSeal Vascular Closure System™-enheter har sålts globalt och 827 843 inom Europeiska ekonomiska samarbetsområdet. Den beräknade reklamationsfrekvensen baserat på global försäljning är 0,046 %. Den totala kundklagomålsfrekvensen är mycket låg. Inga nya risker identifierades som inte ingår i bruksanvisningen och riskdokumentationen.

Förekomsten av oönskade biverkningar visas i **tabell 1.2**. Inga nya oförutsedda, framväxande eller oacceptabla risker identifierades genom klagomålen. Det fanns inga signifikanta öknings av frekvensen eller svårighetsgraden av kända biverkningar.

#### 1.4.6 Övergripande sammanfattning av klinisk prestanda och säkerhet

FemoSeal™ VCS är indicerad för användning vid förslutning av den vanliga femorala arteriella punktionen (arteriotomi) hos patienter som har genomgått perkutan kateterisering med en ingreppshylsa på 2,33 mm (7F) eller mindre. Denna kliniska utvärdering är baserad på en omfattande analys av tillgängliga kliniska data och litteratur före och efter marknadsintroduktion som är relevanta för den avsedda användningen av FemoSeal™ VCS.

En omfattande granskning av publicerad litteratur utfördes under perioden 1 september 2019 till och med 31 augusti 2024. Evidensen inkluderade 29 studier för FemoSeal™ VCS. Evidensen som tillhandahålls i den kliniska utvärderingen drar slutsatsen att produkten är säker och effektiv när den används enligt anvisningarna och att eventuella risker och oönskade biverkningar som kan förknippas med produkten under normala användningsförhållanden utgör acceptabla risker när de vägs mot fördelarna för patienten. Prestandaresultaten för de berörda enheterna



överensstämmer med de som förväntas för denna typ av enhet när den används enligt avsedd användning.

Möjliga biverkningar i samband med användning av FemoSeal™ VCS inkluderar de biverkningar som ofta rapporteras med alternativa metoder för arteriotomiförslutning, t.ex. blödning och hematom. Totalt sett är frekvensen av biverkningar som rapporterats vid användning av FemoSeal™ VCS likartad den frekvens som rapporterats med manuell kompression och liknande kärlförslutningsenheter. Specifikt för blödning och hematom är de rapporterade frekvenserna för FemoSeal™ VCS lägre än de rapporterade frekvenserna för liknande vaskulära förslutningsenheter. Alla rapporterade biverkningar, både från den publicerade litteraturen och från övervakningen efter marknadsintroduktionen, hade identifierats tidigare (se **avsnitt 1.3**).

Befintliga data avseende klinisk säkerhet och prestanda för FemoSeal™ VCS tyder på att patientfördelarna med att använda denna vaskulära förslutningsenhet överväger eventuella risker när den används i enlighet med bruksanvisningen.

Enligt vad som anges ovan visar de data som tillhandahålls för FemoSeal™ VCS överensstämmelsen mellan de data som är relaterade till den utvärderade enheten (t.ex. användningen av enheten, säkerhetsresultat, klinisk prestanda och kliniska fördelar) och identifierar likvärdiga produkter och data relaterade till liknande nyligen utvecklade enheter.

Den jämförande analysen av säkerhetsdata identifierade inga luckor mellan:

- Data som nämns i de senaste rönen
- Data som är specifika för den enhet som utvärderas
- Data som nämns i riskhanteringsdokumentationen
- Data som nämns i märkningen och/eller bruksanvisningen (dvs. återstående risker som ska förmedlas till användaren).

Klinisk säkerhet har visats genom låga frekvenser av komplikationer som identifierats i den publicerade kollegialt granskade kliniska litteraturen, företagssponsrade kliniska studier, granskning av data efter marknadsintroduktionen i kombination med det faktum att produkten inte dragits tillbaka från marknaden. Inga prestandaproblem har upptäckts. Den litteratur som granskades behandlade användning av FemoSeal™ VCS enligt tillverkarens avsedda användning.

### **1.5 Möjliga diagnostiska eller terapeutiska alternativ**

Manuell kompression används traditionellt för att uppnå hemostas vid arteriotomistället efter kärlkateteriseringar. Manuell kompression har förknippats med att patienten varit immobiliserad under långa perioder (upp till 8 timmar efter ett ingrepp) och med betydande obehag och förlängd sjukhusvistelse. En nyligen genomförd systematisk granskning visade att mediantiden för att uppnå hemostas med manuell kompression var 20,8 minuter.<sup>1</sup>

Alternativ till manuell kompression inkluderar externa hemostatiska enheter som applicerar mekanisk kompression på arteriotomistället. Dessa enheter förkortar inte tiden till hemostas eller mobilisering, men minskar personalens behov genom att ersätta manuell kompression med mekanisk kompression. Biverkningsfrekvenser i samband med användning av mekanisk kompression liknar frekvenserna vid manuell kompression.

Vaskulära förslutningsenheter, såsom FemoSeal™ VCS, är utformade för att stänga arteriotomier. De syftar till att minska tiden till hemostas och möjliggöra tidigare mobilisering. I en nyligen genomförd systematisk granskning som omfattade 13 kommersiellt tillgängliga enheter fann man att mediantiden för att uppnå hemostas med en kärlförslutningsenhet var 5,4 minuter.

Mediantiden för hemostas för de enskilda kärlförslutningsenheterna varierade från 1 minut (FemoSeal™ VCS) till 14 minuter, där majoriteten av enheterna krävde mellan 4 och 10 minuter.<sup>1</sup>

Vanliga rapporterade biverkningar i samband med förslutning av arteriotomistället, med manuella kompressioner, externa hemostatiska enheter eller kärlförslutningsenheter, inkluderar hematom, blödning vid åtkomststället, pseudoaneurysm, arteriovenös fistel och infektion. Samma systematiska granskning (34 randomiserade kontrollerade prövningar, 14 401 patienter) fann att biverkningsfrekvenserna var likartade för manuell kompression och användning av kärlförslutningsenheter, med undantag för att blödningen tenderade att öka något med kärlförslutningsanordningar.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Föreslagen användarprofil och utbildning

De avsedda användarna av FemoSeal™ Vascular Closure System är läkare med utbildning som kvalificerar dem att utföra arteriell åtkomst och förslutning för endovaskulära ingrepp genom den gemensamma femoralartären och har deltagit i ett läkarinstruktionsprogram från Terumo Medical Corporation FemoSeal™.

## 1.7 Relevanta harmoniserade och gemensamma standarder

| Standardreferens | Innevarande år för efterlevnad/ rev. | Beskrivning                                                                         |
|------------------|--------------------------------------|-------------------------------------------------------------------------------------|
| ISO 11070        | 2014/AMD1:2018                       | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1 |
| EN ISO 11070     | 2014/A1:2018                         | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1 |

| Standardreferens | Innevarande år<br>för efterlevnad/<br>rev. | Beskrivning                                                                                                                                                              |
|------------------|--------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| FDA Guidance     | 20 maj 2021                                | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                                                     |
| ASTM F2052       | 2015                                       | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment                                 |
| ASTM F2213       | 2017                                       | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment                                             |
| ASTM F2503       | 2020                                       | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                                                           |
| ASTM F2182       | 2019                                       | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging                                    |
| EN ISO 13485     | 2016/A11:2021                              | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 13485        | 2016                                       | Medical devices - Quality management systems - Requirements for regulatory purposes                                                                                      |
| ISO 14644-1      | 2015                                       | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1   | 2015                                       | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2      | 2015                                       | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2   | 2015                                       | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of                                                                            |

| Standardreferens    | Innevarande år<br>för efterlevnad/<br>rev. | Beskrivning                                                                                                                                   |
|---------------------|--------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|
|                     |                                            | cleanroom performance related to air cleanliness by particle concentration                                                                    |
| ISO 14644-3         | 2019                                       | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                      |
| EN ISO 14644-3      | 2019                                       | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                      |
| ISO 14698-1         | 2003                                       | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                         |
| EN ISO 14698-1      | 2003                                       | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                         |
| ISO 14698-2         | 2003/TC1:2004                              | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| EN ISO 14698-2      | 2003/TC 1:2004                             | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data |
| USP <788>           | N/A                                        | PARTICULATE MATTER IN INJECTIONS                                                                                                              |
| EU-farmakopé 2.9.19 | N/A                                        | Particulate Contamination: Sub-Visible Particles                                                                                              |
| IEC 62366-1         | 2015                                       | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| SS-EN 62366-1       | 2015                                       | Medical devices — Part 1: Application of usability engineering to medical devices                                                             |
| EN ISO 14971        | 2019/A11:2021                              | Medical devices — Application of risk management to Medical devices                                                                           |
| ISO 14971           | 2019                                       | Medical devices — Application of risk management to Medical devices                                                                           |

| Standardreferens | Innevarande år<br>för efterlevnad/<br>rev. | Beskrivning                                                                                                          |
|------------------|--------------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| ASTM F1980       | 2016                                       | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1   | 2020                                       | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1      | 2018                                       | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2   | 2006                                       | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2      | 2006                                       | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3   | 2014                                       | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3      | 2014                                       | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4   | 2017                                       | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4      | 2017                                       | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| EN ISO 10993-5   | 2009                                       | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| ISO 10993-5      | 2009                                       | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| EN ISO 10993-6   | 2016                                       | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |
| ISO 10993-6      | 2016                                       | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |
| EN ISO 10993-10  | 2023                                       | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                       |

| Standardreferens | Innevarande år<br>för efterlevnad/<br>rev. | Beskrivning                                                                                                                                      |
|------------------|--------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-10     | 2021                                       | Biological evaluation of medical devices —Part 10:<br>Tests for irritation and skin sensitization                                                |
| EN ISO 10993-11  | 2018                                       | Biological evaluation of medical devices — Part 11:<br>Tests for systemic toxicity                                                               |
| ISO 10993-11     | 2017                                       | Biological evaluation of medical devices — Part 11:<br>Tests for systemic toxicity                                                               |
| EN ISO 10993-12  | 2021                                       | Biological evaluation of medical devices — Part 12:<br>Sample preparation and reference materials                                                |
| ISO 10993-12     | 2021                                       | Biological evaluation of medical devices — Part 12:<br>Sample preparation and reference materials                                                |
| EN ISO 10993-17  | 2009                                       | Biological evaluation of medical devices — Part 17:<br>Establishment of allowable limits for leachable<br>substances                             |
| ISO 10993-17     | 2002                                       | Biological evaluation of medical devices — Part 17:<br>Establishment of allowable limits for leachable<br>substances                             |
| ISO 10993-18     | 2020/A1:2022                               | Biological evaluation of medical devices — Part 18:<br>Chemical characterization of medical device materials<br>within a risk management process |
| EN ISO 10993-18  | 2020/A1:2022                               | Biological evaluation of medical devices — Part 18:<br>Chemical characterization of medical device materials<br>within a risk management process |
| EN ISO 10993-23  | 2021                                       | Biological evaluation of medical devices - Part 23:<br>Tests for irritation                                                                      |
| ISO 10993-23     | 2021                                       | Biological evaluation of medical devices - Part 23:<br>Tests for irritation                                                                      |
| ASTM F2382       | 2018                                       | Standard Test Method for Assessment of Circulating<br>Blood-Contacting Medical Device Materials on Partial<br>Thromboplastin Time (PTT)          |

| Standardreferens | Innevarande år<br>för efterlevnad/<br>rev. | Beskrivning                                                                                                                                                                  |
|------------------|--------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F756        | 2017                                       | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>         | N/A                                        | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>        | N/A                                        | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72   | 2019                                       | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135     | 2014/A1:2019                               | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135        | 2014/A1:2018                               | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7   | 2008/A1:2022                               | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |
| ISO 10993-7      | 2008/A1:2019                               | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                                            |
| SS-EN 556-1      | 2024                                       | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices              |
| EN ISO 11737-1   | 2018/A1:2021                               | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                                        |

| Standardreferens | Innevarande år<br>för efterlevnad/<br>rev. | Beskrivning                                                                                                                                    |
|------------------|--------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11737-1      | 2018/A1:2021                               | Sterilization of health care products —<br>Microbiological methods — Part 1: Determination of<br>a population of microorganisms on products    |
| EN ISO 11138-1   | 2017                                       | Sterilization of health care products - Biological<br>indicators - Part 1: General requirements                                                |
| ISO 11138-1      | 2017                                       | Sterilization of health care products - Biological<br>indicators - Part 1: General requirements                                                |
| EN ISO 11138-2   | 2017                                       | Sterilization of health care products — Biological<br>indicators — Part 2: Biological indicators for ethylene<br>oxide sterilization processes |
| ISO 11138-2      | 2017                                       | Sterilization of health care products — Biological<br>indicators — Part 2: Biological indicators for ethylene<br>oxide sterilization processes |
| EN ISO 15223-1   | 2016                                       | Medical device – Symbols to be used with medical<br>device labels, labeling and information to be supplied<br>– Part 1: General requirements   |
| ISO 15223-1      | 2016                                       | Medical device – Symbols to be used with medical<br>device labels, labeling and information to be supplied<br>– Part 1: General requirements   |
| EN 1041          | 2008/A1:2013                               | Information supplied by the manufacturer of medical<br>devices                                                                                 |
| EN ISO 11607-1   | 2020/A1:2023                               | Packaging for Terminally Sterilized Medical Devices<br>– Part 1: Requirements for Materials, Sterile Barrier<br>Systems and Packaging Systems  |
| ISO 11607-1      | 2019/A1:2023                               | Packaging for Terminally Sterilized Medical Devices<br>– Part 1: Requirements for Materials, Sterile Barrier<br>Systems and Packaging Systems  |
| EN ISO 11607-2   | 2020/A1:2023                               | Packaging for Terminally Sterilized Medical Devices<br>– Part 2: Validation requirements for forming, sealing,<br>and assembly processes       |



| Standardreferens     | Innevarande år<br>för efterlevnad/<br>rev. | Beskrivning                                                                                                                                                                         |
|----------------------|--------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11607-2          | 2019/A1:2023                               | Packaging for Terminally Sterilized Medical Devices<br>– Part 2: Validation requirements for forming, sealing,<br>and assembly processes                                            |
| ASTM D4169           | 2016                                       | Standard Practice for Performance Testing of<br>Shipping Containers and Systems                                                                                                     |
| ASTM<br>F1886/F1886M | 2016                                       | Standard Test Method for Determining Integrity of<br>Seals for Flexible Packaging by Visual Inspection                                                                              |
| ASTM F2825           | 2018                                       | Standard Practice for Climatic Stressing of Packaging<br>Systems for Single Parcel Delivery                                                                                         |
| ASTM F2096           | 2011 (R 2019)                              | Standard Test Method for Detecting Gross Leaks in<br>Medical Packaging by Internal Pressurization (Bubble<br>Test)                                                                  |
| ASTM F88/F88M        | 2015                                       | Standard Test Method for Seal Strength of Flexible<br>Barrier Materials                                                                                                             |
| MDCG 2021-24         | 2021                                       | Guidance on classification of medical devices                                                                                                                                       |
| MDCG 2020-3          | 2020                                       | Guidance on significant changes regarding the<br>transitional provision under Article 120 of the MDR<br>with regard to devices covered by certificates<br>according to MDD or AIMDD |
| MDCG 2020-8          | 2020                                       | Post-market clinical follow-up (PMCF) Evaluation<br>Report Template A guide for manufacturers and<br>notified bodies                                                                |
| MDCG 2020-7          | 2020                                       | Post-market clinical follow-up (PMCF) Plan Template<br>A guide for manufacturers and notified bodies                                                                                |
| MDCG 2020-6          | 2020                                       | Regulation (EU) 2017/745: Clinical evidence needed<br>for medical devices previously CE marked under<br>Directives 93/42/EEC or 90/385/EEC                                          |
| MDCG 2019-9 v1       | 2022                                       | Summary of safety and clinical performance A guide<br>for manufacturers and notified bodies                                                                                         |

| Standardreferens | Innevarande år<br>för efterlevnad/<br>rev. | Beskrivning                                                                                                                                                                                                                                                   |
|------------------|--------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2019-8 v2   | 2020                                       | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15     | 2020                                       | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11     | 2021                                       | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19     | 2021                                       | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4   | 2021                                       | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2      | 2019                                       | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1      | 2019                                       | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7      | 2018                                       | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6      | 2018                                       | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |
| MDCG 2018-4      | 2018                                       | MDCG 2018-4 Annex: UDI database Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                                                                                                  |
| MDCG 2018-3 v1   | 2020                                       | Guidance on UDI for systems and procedure packs                                                                                                                                                                                                               |
| MDCG 2021-25     | 2021                                       | Regulation (EU) 2017/745 - application of MDR requirements to ‘legacy devices’ and to devices placed                                                                                                                                                          |

| Standardreferens    | Innevarande år<br>för efterlevnad/<br>rev. | Beskrivning                                                                                                            |
|---------------------|--------------------------------------------|------------------------------------------------------------------------------------------------------------------------|
|                     |                                            | on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC                               |
| Meddev 2.12-2 Rev 2 | 2012                                       | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2 |

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### 3.0 REVISIONSHISTORIK

| SSCP-revisionsnummer      | Utgivningsdatum | Ändringsbeskrivning                                                   | Revision validerad av anmält organ                                                                                                                                                                                                                                                                          |
|---------------------------|-----------------|-----------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022              | 20 januari 2023 | Initial utgåva, vid MDR CE-certifiering                               | <input checked="" type="checkbox"/> Ja<br>Valideringsspråk: English<br><input type="checkbox"/> Nej (gäller endast implanterbara produkter av klass IIa eller vissa IIb (MDR, artikel 52.4 andra stycket) för vilka SSCP ännu inte har validerats av NB)<br><input type="checkbox"/> Annat (specificera):   |
| SSCP-FS-2023 – Revision 1 | 15 mars 2024    | Uppdaterat för perioden 1 januari 2019 till 31 december 2023.         | <input checked="" type="checkbox"/> Ja<br>Valideringsspråk: English<br><input type="checkbox"/> Nej (gäller endast implanterbara produkter av klass IIa eller vissa IIb (MDR, artikel 52 (4) andra stycket) för vilka SSCP ännu inte har validerats av NB)<br><input type="checkbox"/> Annat (specificera): |
| SSCP-FS-2024 Revision 1   |                 | Uppdaterat för perioden mellan 1 september 2019 till 31 augusti 2024. | <input type="checkbox"/> Ja<br>Valideringsspråk: English<br><input type="checkbox"/> Nej (gäller endast implanterbara produkter av klass IIa eller vissa IIb (MDR, artikel 52 (4) andra stycket) för vilka SSCP ännu inte har validerats av NB)<br><input type="checkbox"/> Annat (specificera):            |

|                            |               |                                                       |                                                                                                                                                                                                                                                                                                                                                             |
|----------------------------|---------------|-------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>Revision 2 | June 20, 2025 | Reviderad baserad på<br>NSAI-frågor för<br>validering | <div><input checked="" type="checkbox"/> Ja<br/>Valideringsspråk: English</div> <div><input type="checkbox"/> Nej (gäller endast<br/>implanterbara produkter av<br/>klass IIa eller vissa IIb (MDR,<br/>artikel 52 (4) andra stycket) för<br/>vilka SSCP ännu inte har<br/>validerats av NB)</div> <div><input type="checkbox"/> Annat (specificera):</div> |
|----------------------------|---------------|-------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|



## Güvenlik ve Klinik Performans Özeti

### FemoSeal™ Vascular Closure System

|                                           |                                                                                              |
|-------------------------------------------|----------------------------------------------------------------------------------------------|
| Üretici Firma                             | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 ABD          |
| Üretici firmanın tek kayıt numarası (SRN) | US-MF-000019594                                                                              |
| Management Representative/PRRC            | Kimberly Feitl<br>Vice President, Kalite                                                     |
| Temel UDI-DI                              | 38970FS79                                                                                    |
| EMDN numarası                             | C900199 - Hemostaz Sistemleri-Diğer                                                          |
| Cihaz Sınıfı                              | Sınıf III                                                                                    |
| Cihazın İlk CE İşaretinin Alındığı Yıl    | 2005                                                                                         |
| AB Temsilcisi                             | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belçika<br>SRN: BE-AR-000001433 |
| Onaylanmış Kuruluş                        | NSAI<br>CE 0050                                                                              |

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Bu Güvenlik ve Klinik Performans Özeti (SSCP), FemoSeal™ Vascular Closure System (VCS) cihazının güvenlik ve klinik performansının ana yönlerinin güncellenmiş bir özetine genel erişim sağlamayı amaçlamaktadır.

Cihazın kullanıcılarına/sağlık uzmanlarına yönelik güvenlik ve klinik performans özeti aşağıdaki **Bölüm 1.0'**da verilmiştir.

## 1.0 KULLANICILAR / SAĞLIK UZMANLARI İÇİN ÖZET

SSCP, cihazın güvenli kullanımını sağlamaya dair asıl belge olan Kullanım Talimatlarının yerine kullanılamaz ve kullanıcılara veya hastalara tanısal veya terapötik öneriler sunmayı amaçlamamaktadır. SSCP, implant kartlarındaki veya diğer zorunlu belgelerdeki zorunlu bilgilerin yerini almak üzere tasarlanmamıştır.

### 1.1 Cihazın Kullanım Amacı

#### 1.1.1 Kullanım Amacı

FemoSeal™ Vascular Closure System, ortak femoral arter yoluyla perkütan kateterizasyondan sonra arter ponksiyonunun kapatılması için tasarlanmış tıbbi bir cihazdır.

#### 1.1.2 Kullanım Talimatları

FemoSeal™ Vascular Closure System, 7F (2,33 mm) veya daha küçük bir prosedür kılıfı kullanılarak perkütan kateterizasyon yapılan hastalarda ortak femoral arter ponksiyonunun (arteriyotomi) kapatılmasında kullanılmak üzere endikedir.

#### 1.1.3 Kontrendikasyonlar ve/veya Sınırlamalar

FemoSeal™ Vascular Closure System, 7F (2,33 mm)'den daha büyük kılıf veya cihazların kullanıldığı arteriyotomileri olan hastalarda kontrendikedir.

#### 1.1.4 Hedef Hasta Popülasyonu

FemoSeal™ Vascular Closure System cihazının güvenilirliği ve etkinliği, 18 yaş ve üzeri, 7F (2,33 mm) veya daha küçük bir prosedür kılıfı kullanılarak perkütan kateterizasyon uygulanan hastalarda belirlenmiştir.

#### 1.1.5 Özel Hasta Popülasyonları

FemoSeal™ Vascular Closure System cihazının güvenliği ve etkinliği aşağıdaki hasta popülasyonlarında belirlenmemiştir:

- Önceden otoimmün hastalığı olan hastalar.
- Terapötik tromboliz uygulanan hastalar.
- Klinik olarak anlamlı periferik vasküler hastalığı olan hastalar.
- Kontrolsüz hipertansiyona sahip hastalar (> 220 mmHg sistolik veya > 110 mmHg diyastolik).
- Trombositopeni (< 100.000 trombosit sayımı) veya anemi (Hgb < 10 mg/dl) dahil olmak üzere kanama bozukluğu olan hastalar.

- Ortak femoral arterin iç lümeni 5 mm'den küçük olan hastalar.
- Böbrek ve/veya hepatik bozukluğu olan hastalar.
- Diğer ilgili komorbiditeli hastalar.
- Spesifik ırk ve/veya etnik kökenli nüfus.
- 72 saat içinde miyokard enfarktüsü olan hastalar.
- Ponsiyon alanında vasküler greft veya stent bulunan hastalar.
- Hamile veya emziren hastalar.
- 18 yaşından küçük hastalar.

### 1.1.6 Amaçlanan Kullanıcılar

FemoSeal™ Vascular Closure System cihazının amaçlanan kullanıcıları, ortak femoral arter yoluyla endovasküler prosedürler için arteriyel erişim ve kapama gerçekleştirme konusunda eğitim almış ve Terumo Medical Corporation FemoSeal™ doktor eğitim programına katılmış doktorlardır.

## 1.2 Cihaz Açıklaması

### 1.2.1 Cihazın Açıklaması

Terumo Medical Corporation (TMC) tarafından üretilen FemoSeal™ Vascular Closure System, ortak femoral arter yoluyla perkütan kateterizasyondan sonra femoral arteriyel hemostaz sağlamak için tasarlanmış, yeniden emilebilir bir vasküler kapama cihazıdır.

FemoSeal™ kapatma elemanları, emilebilen multifilaman ile bir arada tutulan iç kapak ve dış kilitleme diski olmak üzere iki emilebilir polimer diskten oluşur ve bu sayede arteriyotominin mekanik olarak kapatılmasını sağlar (bk. **Şekil 1.1** ve **Şekil 1.2**). Koni muhafaza kılıfı yoluyla yerleştirildikten sonra, dış kilitleme diski multifilaman şaft üzerine sıkıştırılır ve iç ve dış kilitleme diski arasındaki delinme bölgesinin mekanik olarak kapatılmasını sağlar. İç kapak ve dış kilitleme diski, multifilaman şaft üzerindeki sürtünme yoluyla yerinde tutulur. Hemostaz mekanik yollarla elde edilir. Kapatma elemanları hidroliz ile bozunur.

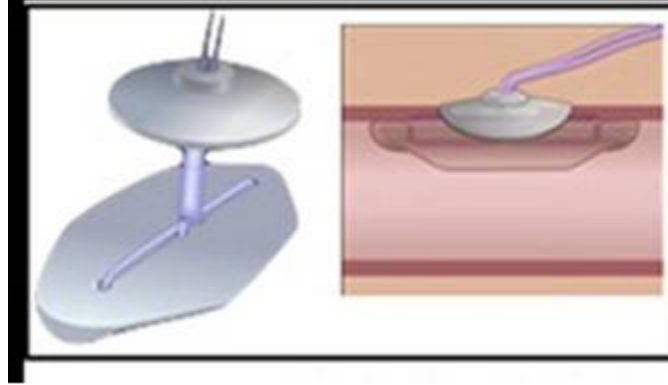
İmplant edilebilir kapatma bileşenleri, iç kapak ve dış kilitleme diski, on sekiz (18) ay içinde bozunurken multifilamanın iki (2) ila üç (3) yıl sonra çevre doku tarafından hidrolizle bozulacağı ve absorbe edileceği tahmin edilir. İmplant edilebilir kapatma bileşenlerinin arteriyotomi üzerindeki kompresyonu koruma becerisi sekiz (8) saate kadar test edilmiştir. Degradasyon ürünleri metabolize edilir ve idrarda atılır veya akciğerler aracılığıyla karbondioksit olarak ekspirasyon yapılır. Hayvanlar üzerinde yapılan araştırmalarda birikim etkisi gözlenmemiştir.

İşlem sırasında canlı doku veya kanla temas edecek FemoSeal™'in ek bileşenleri; koni muhafaza kılıfı, dilatör, sıkıştırma tüpü, itici ve kılavuz teldir.

**Şekil 1.1 Sırasıyla İç Kapak ve Dış Kilitleme Diski**

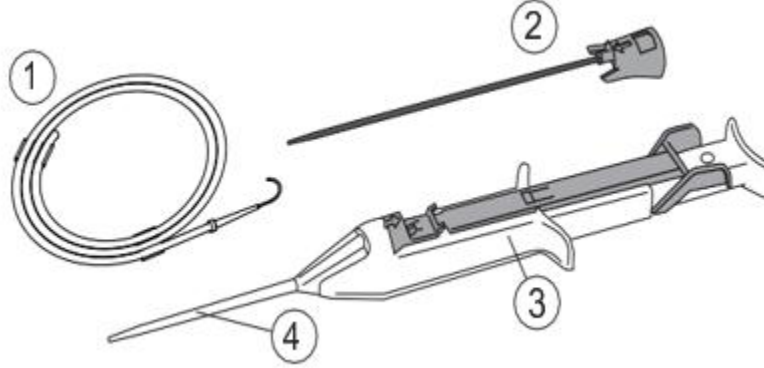


**Şekil 1.2 Yerleştirilmiş İç Kapak ve Dış Kilitleme Diski**



FemoSeal™ ünitesi bir dilatör ve 0,038 inç (0,97 mm) DÇ, 27,5 inç (70 cm) uzunlukta bir kılavuz tel ve bir J düzleştirici ile birlikte paketlenmiştir, aşağıdaki **Şekil 1.3**'e bakın. Kılavuz tel, polietilen bir tüp içinde bulunur. Tüm parçalar sabit bir kağıt tepside paketlenmiştir. Paket ayrıca hasta implant kartını da içerir. FemoSeal™ Vascular Closure System, cihazın amaçlandığı gibi çalışması için ek aksesuarlar gerektirmez ve cihaz sadece ürünün ambalajında bulunan dilatör ve kılavuz tel ile kullanılmak üzere tasarlanmıştır.

### Şekil 1.3 FemoSeal™ VCS Ünitesi ile Kılavuz Tel ve Dilatör



#### 1.2.2 Ham Maddeler ve Bileşenler

Aşağıdaki Tablo 1.1'de FemoSeal™ VCS'nin bileşenleri listelenmiştir.

**Tablo 1.1 FemoSeal™ VCS Ham Maddeleri ve Bileşenleri**

| Parça Numarası | Açıklama                                                          | Materyaller                                                                                                                                                                                                                                                                                        |
|----------------|-------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1              | 0,038 inç (0,97 mm) Kılavuz tel, kılavuz tel J düzleştiricisi ile | Kılavuz Tel 304 Paslanmaz Çelik<br>J-Düzleştirici: Polipropilen, mor pigment<br>Kelepçe: Polietilen<br>Boru sistemi: Polietilen                                                                                                                                                                    |
| 2              | FemoSeal Dilatör                                                  | Göbek Tetrahidrofuran, Mavi pigment, Polibütil tereftalat (PBT)<br><br>Tüp: Yüksek yoğunluklu polietilen (HDPE), siyah pigment<br><br>Yağlayıcı: Silikon Dow Corning 360                                                                                                                           |
| 3/4            | FemoSeal Ünitesi                                                  | Kalıplı RD7 - İç Kapak ve Dış Kilitleme Diski*                                                                                                                                                                                                                                                     |
|                | Multifilaman *                                                    | Glikolit, trimetilen karbonat, ε-kaprolakton ve TMP arasındaki kopolimer: trimetilolpropan (initiatör)<br><br>L, L-Laktid, trimetilen karbonat, ε-kaprolakton ve 1,3 propanediol (initiatör) arasında segmentli kopolimer<br><br>Kaplama, glikolit, ε-kaprolakton ve L-lisin arasında kopolimerdir |



|  |  |                      |                                                 |
|--|--|----------------------|-------------------------------------------------|
|  |  | Sıkıştırma Tüpü      | Polipropilen                                    |
|  |  | İtici                | 304V Paslanmaz Çelik                            |
|  |  | Kaydırma çubuğu      | Polibütül tereftalat (PBT)                      |
|  |  | Muhafaza             | Polibütül tereftalat (PBT)                      |
|  |  | Düğme                | Polibütül tereftalat (PBT)                      |
|  |  | Düğme Kapağı         | Polioksimetilen (POM)/Poliasetal Kopolimer      |
|  |  | Kılıf                | Polibütül tereftalat (PBT)                      |
|  |  | Aralayıcı            | Polibütül tereftalat (PBT)                      |
|  |  | Koni                 | Polipropilen                                    |
|  |  | Gövde Kapağı         | Polibütül tereftalat (PBT)                      |
|  |  | Güvenlik Tutucusu    | Polibütül tereftalat (PBT), mavi pigment        |
|  |  | Kılıf Kapağı         | Polibütül tereftalat (PBT)                      |
|  |  | Tüp Contası          | Silikon shore A 70                              |
|  |  | Muhafaza Contası     | Silikon shore A 50                              |
|  |  | Yay                  | 302 Paslanmaz Çelik                             |
|  |  | Koni Muhafaza Kılıfı | Polipropilen<br>Silikon Dow Corning 360, Heksan |

\* Cihazın implante edilebilir kısmı; implante edilebilir bileşenler MRG için tehlike oluşturmazlar

FemoSeal™ VCS Etilen Oksit (EO) ile sterilize edilmiştir ve tek kullanımlık bir tıbbi cihazdır. FemoSeal™ VCS cihazı tekrar kullanılamayacak şekilde tasarlanmıştır.

### **Eylem Modu**

FemoSeal™ VCS, sık kullanılan femoral arterin içine ve dışına implante edilebilir kapatma elemanları uygulayarak mekanik hemostazı destekler. Kanamayı önleyen mekanizma, delme alanını kapatan iç kapak ve iç kapağı yerinde tutan dış kilitleme diski ile sağlanır.

### **1.2.3 Klinik Fayda**

FemoSeal™ VCS ortak femoral arter ponksiyonundan sonra vasküler kapamayla ilgili olarak aşağıdaki klinik faydaları sağlar:

- Hemostaz süresini kısaltma<sup>1</sup>
- Ambülasyon süresini kısaltma<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

#### 1.2.4 Önceki Nesil(ler) veya Varyantlar

- FemoSeal™ VCS'in ilk sürümü (#11200), 2005 yılında ve 2006 yılının bir kısmında Avrupa pazarında satılmıştır.
- Geliştirilmiş bir uygulama sistemine sahip mevcut FemoSeal™ VCS (#11202), 28 Mart 2006'dan beri piyasada.

#### 1.2.5 Cihazla Birlikte Kullanılması Amaçlanan Aksesuarlar

FemoSeal™ ünitesi bir dilatör, 0,038 inç (0,97 mm) DÇ, 27,5 inç (70 cm) uzunluğunda bir kılavuz tel ve bir J düzleştirici ile birlikte paketlenir. Kılavuz tel, FemoSeal™ ünitesinin bir aksesuarıdır. J-düzleştirici, kılavuz telin bir bileşenidir, dilatör ise FemoSeal™ ünitesinin bir bileşenidir. Kılavuz tel, dikkate alınan tek aksesuardır. Kılavuz tel, polietilen bir tüp içinde bulunur. Tüm parçalar sabit bir kağıt tepside paketlenmiştir. Paket ayrıca hasta implant kartını da içerir. FemoSeal™ Vascular Closure System, cihazın amaçlandığı gibi çalışması için ek aksesuarlar gerektirmez ve cihaz sadece ürünün ambalajında bulunan dilatör ve kılavuz tel ile kullanılmak üzere tasarlanmıştır.

#### 1.2.6 Cihazla Birlikte Kullanılması Amaçlanan Diğer Cihazlar ve Ürünler

FemoSeal™ VCS'nin amaçlanan şekilde çalışması için ek cihazlar gerekmez.

### 1.3 Riskler ve Uyarılar

#### 1.3.1 Rezidüel Riskler ve İstenmeyen Etkiler

FemoSeal™ VCS'nin kullanımıyla ilişkili olan ve rezidüel riskten kaynaklanan, bilinen veya öngörülebilir advers olaylar, zararlar ve komplikasyonlar **Tablo 1.2'**de listelenmiştir. Oluşma oranı, Risk Dokümantasyonu'nun analizine dayanır ve 1 Eylül 2019 - 31 Ağustos 2024 tarihleri arasındaki Pazarlama Sonrası Gözetim verilerine göre hesaplanır. FemoSeal™ VCS'ye ilişkin herhangi bir bilinmeyen rezidüel risk bulunmamaktadır ve tüm geçerli riskler Kullanım Talimatları ve risk yönetim süreci yoluyla ele alınmıştır.

**Tablo 1.2. FemoSeal Advers Olaylar/Komplikasyonlar**

| Zarar                                   | Oluşma Oranı (%) | Azaltıcı Faktörler                                                                                                                                                |
|-----------------------------------------|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Alerjik reaksiyon                       | 0,0000           | Riski mümkün olduğunca azaltmaya yönelik eylemler ve planlar; ürün tasarım özellikleri, üretim kılavuzları, ürün etiketleme ve doktor eğitimi ile ele alınmıştır. |
| Anevrizma                               | 0,0000           |                                                                                                                                                                   |
| AV fistül                               | 0,0001           |                                                                                                                                                                   |
| Kan kaybı / kanama                      | 0,0280           |                                                                                                                                                                   |
| Ölüm                                    | 0,0002           |                                                                                                                                                                   |
| Ekimoz                                  | 0,0000           |                                                                                                                                                                   |
| Emboli                                  | 0,0000           |                                                                                                                                                                   |
| Yabancı cisim reaksiyonu                | 0,0000           |                                                                                                                                                                   |
| Hematom                                 | 0,0027           |                                                                                                                                                                   |
| Hemoraj                                 | 0,0001           |                                                                                                                                                                   |
| Enfeksiyon                              | 0,0002           |                                                                                                                                                                   |
| Enflamatuvar reaksiyon                  | 0,0000           |                                                                                                                                                                   |
| Uyuşukluk                               | 0,0000           |                                                                                                                                                                   |
| Ağrı                                    | 0,0000           |                                                                                                                                                                   |
| Hastanın rahatsızlığı                   | 0,0004           |                                                                                                                                                                   |
| Prosedür gecikmesi                      | 0,0065           |                                                                                                                                                                   |
| Psödoanevrizma                          | 0,0004           |                                                                                                                                                                   |
| Retroperitoneal kanama                  | 0,0002           |                                                                                                                                                                   |
| Sepsis                                  | 0,0000           |                                                                                                                                                                   |
| Tromboembolizm                          | 0,0000           |                                                                                                                                                                   |
| Tromboz                                 | 0,0001           |                                                                                                                                                                   |
| Damar oklüzyonu/alt ekstremite iskemisi | 0,0002           |                                                                                                                                                                   |
| Damar perforasyonu                      | 0,0000           |                                                                                                                                                                   |
| Damar dokusu diseksiyonu/laserasyonu    | 0,0003           |                                                                                                                                                                   |

### 1.3.2 Uyarılar ve Önlemler

#### Uyarılar

1. Paket hasar görmüşse veya steril bariyerlerden herhangi biri sağlam değilse kullanmayın.
2. Son kullanma tarihinden sonra kullanmayın. Biyolojik olarak bozunabilir bileşenler yeterli bir şekilde çalışmayabilir.
3. Herhangi bir ögenin hasarlı veya kusurlu görünmesi durumunda kullanmayın.
4. FemoSeal™ Vascular Closure System cihazının, prosedür kılıfında veya etrafındaki dokuda bakteriyel kontaminasyonun enfeksiyona neden olabileceği durumlarda kullanılması.
5. Posterior arteriyel duvarın delindiğinden veya birden fazla delinme olduğundan şüpheleniliyorsa, arteriyel hemostazın sağlanmasında yalnızca FemoSeal™ Vascular Closure System cihazına güvenmeyin. İlave manuel veya mekanik kompresyon kullanın.
6. Ponksiyon bölgesi femoral arter bifurkasyonundaysa veya buna distal konumdaysa, İç Kapağın yanlış yerleştirilmesi riski nedeniyle FemoSeal™ Vascular Closure System kullanılmamalıdır. Bu olay, kanama komplikasyonlarına ve/veya normal kan akışında bozulmaya neden olabilir.
7. İnsizyon bölgesinden sürekli arteriyel kanama varsa, hemostaz sağlanana kadar multifilamanı kesmeyin. Hemostaz sağlanamazsa, multifilamanı steril yara sargısıyla sabitleyin ve hemostaz sağlanana kadar ek kompresyon uygulayın. Devam eden arteriyel kanama durumunda, önemli kanama komplikasyonları meydana gelebilir ve bu da hastanın yaralanmasına veya ölümüne neden olabilir.
8. Delinme bölgesi inguinal ligamente proksimal ise FemoSeal™ Vascular Closure System cihazını kullanmayın, çünkü bu retroperitoneal hematoma neden olabilir.
9. Kanama riski daha yüksek olan hastalar artan kan kaybı yaşayabilir ve transfüzyon gerektirebilir.
10. İç diskin ayrılması trombotik ve/veya embolik bir olaya yol açabilir.

#### Önlemler

1. FemoSeal™ Vascular Closure System yerleştirme prosedürü, cihazın kullanımı konusunda yeterli eğitime sahip doktorlar tarafından gerçekleştirilmelidir.
2. FemoSeal™ Vascular Closure System cihazının yerleştirilmesinden önce sınırlı bir femoral anjiyogram veya ultrason kılavuzlu femoral ponksiyon gerçekleştirin.
3. Aşağıdaki durumlarda prosedürü durdurun:
  - Ortak femoral arterin lümen çapı 5 mm'den küçük ise.

- Ortak femoral arter ponksiyon bölgesi yakınında stenoz ve/veya önemli plak bulunması.
  - Arteriyel ponksiyon, femoral arter bifurkasyonunda veya distalindedir.
  - Ortak femoral arter ponksiyon bölgesinin yakınında anormal dallar veya damar anormallikleri var.
4. Herhangi bir hematoma varsa, koni muhafaza kılıfının artere doğru yerleştirilmesine özellikle dikkat edilmelidir.
  5. Tek duvar delme tekniđi kullanın. Arterin posterior duvarını delmeyin.
  6. FemoSeal™ Vascular Closure System cihazını kullanırken her zaman steril tekniklere uyun.
  7. FemoSeal™ Vascular Closure System yalnızca tek kullanımlıktır ve hiçbir şekilde yeniden sterilize edilmemeli veya yeniden kullanılmamalıdır. FemoSeal™ ünitesi, tekrar kullanılamayacak şekilde tasarlanmıştır.
  8. İç Kapağın takılması beklenmedik bir dirençle karşılaşırsa, prosedürü bırakın.
  9. İç Kapağın doğru şekilde takılması için başparmağınızı, düğme serbest şekilde geri yayanabilecek şekilde yeniden konumlandırın.
  10. Dış Kilitleme Diski'ni yerleştirmeden önce FemoSeal™ Ünitesi'nin koni muhafaza kılıfının ucunun cilt yüzeyinin altında olduğundan emin olun. Dış Kilitleme Diski, femoral arter ile cilt seviyesi arasında kısa bir mesafe olan hastalarda, yanlışlıkla cilt seviyesinin üzerinde yerleştirilebilir.
  11. Doğru yerleştirme için yerleştirmeden önce bir deri insizyonu gerekli olabilir.
  12. İç Kapak arterin içindeyse, ancak düğmeye tam olarak basmak ve Dış Kilitleme Diskini yerleştirmek mümkün değilse, FemoSeal™ Kapatma Ögelerini çıkarmak için ameliyat gerekebilir.
  13. 18 ay içinde aynı femoral arterin tekrar delinmesi gerekirse, yeni delik, önceki FemoSeal™ Vascular Closure System erişim bölgesine en az bir santimetre proksimal olacak şekilde açılmalıdır.
  14. Hastadan, kapatma sahasının incelenmesiyle ilgili olarak doktorun talimatlarına uymasını isteyin.
  15. Hastadan, gelecek 18 ay için Hasta Bilgi Kartını taşımasını isteyin

### **Taburculuk işlemi sırasında alınacak önlemler**

Taburculuk işlemi göz önünde bulundurmadan önce hastayı aşağıdaki klinik durumlar açısından değerlendirin:

1. Kapatma alanında kanama ve/veya hematoma.
2. Yürürken ağrı oluşması.
3. Kapatma alanında enfeksiyon belirtileri.

### **1.3.3 Saha Güvenliği Düzeltici Faaliyetleri**

1 Eylül 2019 ile 31 Ağustos 2024 arasında FemoSeal™ VCS'yi içeren bir Saha Güvenliği Düzeltici Faaliyeti vardı.

Terumo, 2022 yılında, Elkton tarafından üretilen FemoSeal ürününün Sıkıştırma Kuvveti Ölçümü ve Retraksiyon Kuvveti ile ilgili proses ve parti piyasaya sürme testini geçemediğini öne süren şikâyetler nedeniyle FemoSeal™ VCS'yi gönüllü olarak geri çağırdı. Güney Kore'den toplam 950 adet ünite geri çağırıldı.

### **1.4 Klinik Değerlendirme ve Pazarlama Sonrası Klinik Takip**

**Tablo 1.3'te** FemoSeal™ VCS'yi piyasaya sunmanın yanı sıra pazarlama sonrası çalışmalara ve pazarlama sonrası klinik takip faaliyetlerine götüren önemli çalışmaların bir listesi yer almaktadır. Çalışmada kullanılan cihazın sürümü aşağıdaki tabloda verilmiştir. FemoSeal™ VCS'in (#11200) ilk sürümü 2006 yılına kadar piyasadaydı, bir sonraki sürüm (#C11202) 2006 yılında piyasaya sürüldü ve günümüzde piyasada bulunan bir sürümdür.

**Tablo 1.3 Önemli Çalışmaların Özeti**

| <b>Pazarlama Öncesi Fonksiyonel Hayvan Testi</b>                                                                                                                                                                                                                        | <b>Cihaz Sürümü</b>      |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                    |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                    |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                    |
| <b>İnsanlarda İlk Klinik Çalışma</b>                                                                                                                                                                                                                                    |                          |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                    |
| <b>Tamamlanan Pazarlama Sonrası Klinik Çalışmalar</b>                                                                                                                                                                                                                   |                          |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                                                                              | C11202<br>(mevcut cihaz) |

|                                                                                                                                 |                          |
|---------------------------------------------------------------------------------------------------------------------------------|--------------------------|
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                               | C11202<br>(mevcut cihaz) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                  | C11202<br>(mevcut cihaz) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)          | C11202<br>(mevcut cihaz) |
| <b>Planlanan / Devam Eden Pazarlama Sonrası Klinik Çalışmalar</b>                                                               |                          |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                      | C11202<br>(mevcut cihaz) |
| <b>Pazar Sonrası Klinik Takip Faaliyetleri</b>                                                                                  |                          |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(mevcut cihaz) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(mevcut cihaz) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(mevcut cihaz) |

#### 1.4.1 Pazarlama Öncesi Verilerin Özeti (Hayvan Testi ve Klinik Araştırmalar)

Aşağıdaki **Tablo 1.4**'te hem hayvan testi hem de klinik araştırmalar dâhil tüm pazarlama öncesi çalışmalar açıklanmaktadır.

**Tablo 1.4 Pazarlama Öncesi Çalışmaların Özetleri**

| <b>Pazarlama Öncesi Fonksiyonel Hayvan Testi</b>                                                                                                                                                                                                                        |                                                                                     |                                     |                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Çalışma Başlığı</b>                                                                                                                                                                                                                                                  | <b>Yıl / CI</b>                                                                     | <b>Çalışma Türü</b>                 | <b>Amaçlar</b>                                                                                                                                                                                                                                              | <b>Önemli Olaylar</b>                                                                                                                                                                                                                                                                    | <b>Potansiyel Kabul Edilme Kriterleri</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 2000<br>Radi Medical System AB<br><br>Biomatech, Fransa tarafından gerçekleştirildi | Hayvan çalışması; Keşif araştırması | Çalışmanın amacı, vasküler sistemde hemostaz yapmak için tasarlanmış biyolojik olarak parçalanabilen bir implantın biyouyumluluğunu ve biyoilevselliğini değerlendirmektir. Rapor, Çalışma Numarası 862'den kalan hayvanlara yöneliktir (Belge No. 1051-01) | N = 3 yetişkin dişi koyun, zaman noktası başına 1 hayvan<br><br>Histopatolojik analiz, makroskopik derecelendirme ve ultrayapısal analiz için takip<br><br>• 12 ay<br>• 15 ay<br>• 18 ay<br><br>Renkli doppler ultrason takibi - karotid ve femoral arteriyel erişim bölgelerinde 30 gün | Arteriyel açıklık<br>• Uygulama sonrası kan akışı değerlendirmesi. Her ikisi de sol ortak karotid arterde meydana gelen, prosedürle ilgili geçici arteriyel vazospazm ile ilişkili 3 vakanın 2'sinde kan akışı azalması<br>• Renkli doppler ultrason değerlendirmesi (4 hafta). İmplantasyondan 30 gün sonra 3 vakanın 3'ünde (%100) majör kan akışı azalması olmadan<br><br>Makroskopik gözlemler<br>• 12 ay - patensi, anatomik olarak görünür oklüzyon olmamasıyla makroskopik olarak doğrulanmıştır; |

|                                                                                                                 |                             |                                     |                                                                                                           |                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|-----------------------------------------------------------------------------------------------------------------|-----------------------------|-------------------------------------|-----------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                 |                             |                                     |                                                                                                           |                                                                                                                          | <p>makroskopik lokal intolerans lezyonları (hemoraj, nekroz veya neovaskülerizasyon) yoktur; iç disk kapsülünün işaretlendiği görülmektedir</p> <ul style="list-style-type: none"><li>15 ay - makroskopik gözlem enflamasyon belirtisi göstermedi; iç ve dış disklerde tanımlanan kalıntı yok; dış disk alanında bulunan enkapsülasyon dokusu 12 aylık gözlemlerle aynı görünüyordu</li><li>18 ay - makroskopik gözlemlerde lokal intolerans belirtisi görülmedi, dış disk görüldü (3/3 vaka), iç diskte degradasyon tamamlandı; 3 vakanın 1'inde (sol ortak karotid arteri) - implant bölgesinde gözlenen arter duvarında depresyon (cihazın yerleştirilmesiyle ilgili olabilir)</li></ul> <p>Varılan Sonuçlar</p> <ul style="list-style-type: none"><li>Makroskopik olarak, implantasyondan 12, 15 ve 18 ay sonra nekrotik, dejeneratif veya trombotik belirtiler saptanmamıştır.</li><li>İç ve dış disklerin degradasyon süreci 12 ila 18 ay arasında ilerlemiş ve 18 ayda dikişler tamamlanmış, implante edilen alanı kaplayan beyazımsı bir doku görünmüştür.</li><li>Histolojik olarak, 18 ay sonra polimer materyal artık görünmez durumdaydı, ancak endoluminal fibröz doku mevcuttu. Nekrotik, dejeneratif veya trombotik lezyonlar görülmemiştir.</li></ul> |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. | 2002 Radi Medical System AB | Hayvan çalışması; Keşif araştırması | Çalışmanın amacı, vasküler sistemde hemostazı sağlamak için kodlanmış biyoçözünür bir implantın biyolojik | Takip (implantasyondan sonra) <ul style="list-style-type: none"><li>12 hafta</li><li>24 hafta</li><li>36 hafta</li></ul> | <u>4 hafta sonra karotid ve femoral arterlerin açıklığı</u> <ul style="list-style-type: none"><li>Önemli kan akışı azalması 0/12 (%0)</li></ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |



|                                                                                                                                                         |                                               |  |                                   |                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
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| Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | Biomatech, Fransa tarafından gerçekleştirildi |  | uyumluluğunu değerlendirmektedir. | <p>N = 12 koyun, zaman noktası başına 3 hayvan, 12, 15 ve 18 ayda feda edilen kalan 3 hayvan</p> <p>İmplantasyon bölgeleri - sağ ve sol femoral arterler, sağ ve sol ortak karotid arterler</p> <p>Renkli doppler ultrason analizi</p> | <p><u>Kan akışında önemli bir azalma yok</u></p> <ul style="list-style-type: none"> <li>Cihaz yerleştirilmesiyle ilgili ciddi kan akışı bozukluğu 0/12 (%0)</li> <li>Geçici arteriyel vazospazm nedeniyle sol ortak karotidde 12 vakanın 2'sinde (%16,6) kan akımının azalması (cihaza değil cerrahiye atfedilir)</li> </ul> <p><u>Takip zamanında kan akışı bozukluğu</u></p> <p>12 hafta - 0/12 (%0)<br/>24 hafta - 0/12 (%0)<br/>36 hafta - 0/12 (%0)</p> <p>Tansiyon ölçümü (3 koyun - 36 hafta)</p> <ul style="list-style-type: none"> <li>Kan akışında önemli bir azalma algılanmadı</li> </ul> <p>Entegrasyon ve degradasyon için makroskopik veriler (Sınıf 0-4)</p> <p><u>Karotid alanlar</u></p> <p><i>Dahili taraf</i></p> <p>-kapsülleme</p> <p>12 hafta 1,3<br/>24 hafta 0,8<br/>36 hafta 0,7</p> <p>-malzeme degradasyonu</p> <p>12 hafta 2,2<br/>24 hafta 2,3<br/>36 hafta 0,7</p> <p><i>Harici taraf</i></p> <p>-kapsülleme</p> <p>12 hafta 2,0<br/>24 hafta 1,0<br/>36 hafta 0,8</p> <p>-malzeme degradasyonu</p> <p>12 hafta 2,0<br/>24 hafta 2,7<br/>36 hafta 3,2</p> <p><u>Femoral alanlar</u></p> <p><i>Harici taraf</i></p> <p>-kapsülleme</p> <p>12 hafta 1,0<br/>24 hafta 2,7</p> |
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|  |  |  |  |  | <p>36 hafta 1,0<br/>-malzeme degradasyonu<br/>12 hafta 2,0<br/>24 hafta 2,4<br/>36. hafta 3,0</p> <p><i>Dahili taraf</i><br/>-kapsülleme<br/>12 hafta 2,0<br/>24 hafta 1,2<br/>36 hafta 1,0<br/>-malzeme degradasyonu<br/>12 hafta 1,0<br/>24 hafta 2,2<br/>36. hafta 3,0</p> <p><u>Entegrasyon, degradasyon ve enflamatuvar parametreler için histolojik veriler (ilgili değerlerin ortalaması, İndeks 0-4) n=6</u></p> <p><u>Karotid alanlar</u><br/>Harici fibrozis<br/>12 hafta - 2,3<br/>24 hafta - 2,3<br/>36 hafta - 1,8<br/>Dahili neointima<br/>12 hafta - 3,0<br/>24 hafta - 2,7<br/>36 hafta - 3,3<br/>Malzeme degradasyonu<br/>12 hafta - 1,7<br/>24 hafta - 3,0<br/>36 hafta - 3 +<br/>Enflamatuvar parametreler (makrofajlar)<br/>12 hafta - 3,0<br/>24 hafta - 1,7<br/>36 hafta - 1,7</p> <p><u>Femoral alanlar</u><br/>Harici fibrozis<br/>12 hafta - 1,3<br/>24 hafta - 1,5<br/>36 hafta - 1,7<br/>Dahili neointima<br/>12 hafta - 3,7<br/>24 hafta - 3,3<br/>36 hafta - 3,8<br/>Malzeme degradasyonu<br/>12 hafta - 2,0</p> |
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|                                                                                                                            |                                |                  |                                                                                                                                       |                                                                                      | <p>24 hafta - 3,0<br/>36 hafta - 3+<br/>Enflamatuvar parametreler (makrofajlar)<br/>12 hafta - 3,5<br/>24 hafta - 1,8<br/>36 hafta - 1,8</p> <p><u>Histomorfolojik açıklık değerleri</u><br/>Karotid alanlar<br/>12 hafta %74,0<br/>24 hafta %81,9<br/>36 hafta -%89,43<br/>Femoral alanlar<br/>12 hafta - %42,2<br/>24 hafta - %73,21<br/>36 hafta - %78,71</p> <p><u>US damar açıklığı (ortalama %)</u><br/>Karotid alan<br/>12 hafta %94,6<br/>24 hafta - %96,7<br/>36 hafta - %94,7<br/>Femoral alanlar<br/>12 hafta - %66,9<br/>24 hafta - %63,6<br/>36 hafta - %75,1</p> <p>Varılan Sonuçlar</p> <ul style="list-style-type: none"> <li>12, 24 veya 36 haftada belirgin bir lokal intolerans işareti saptanmamıştır (görünür enflamatuvar, nekrotik veya dejeneratif lezyonların olmaması)</li> <li>Konakçı ve cihaz ile ilgili olarak kayda değer bir advers dokusal reaksiyon kaydedilmemiştir</li> <li>İmplantın degradasyonu neredeyse 36 haftada tamamlandı</li> </ul> |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional | 2002<br>Radi Medical System AB | Hayvan çalışması | Çalışmanın amacı, vasküler sistemde hemostaz yapmak için tasarlanmış biyolojik olarak parçalanabilen bir implantın biyoyumluluğunu ve | İmplantasyon periyodu / takibi tüm hayvanlar için 5 haftadır<br><br>4 koyun, 1 domuz | Herhangi bir advers bulgu kriteri (inflamasyon, nekroz, kanama veya başka herhangi bir lezyon) veya herhangi bir ince psödo-intimal tabaka oluşumu kaydedilmedi.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |

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| Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France). | Biomatech, Fransa tarafından gerçekleştirildi |  | biyoilevselliğini değerlendirmektir. Test edilen cihaz, hemostazın sağlanması için arterlerdeki ponksiyon deliğine girmeye yöneliktir. Bir disk arterdeki ponksiyon deliğine girmiştir, diğer disk arterin dışından dâhili diski sıkıştırmıştır. Her iki disk bir giriş seti kılıfının içinden geçirilmiştir. Diskler kanamayı önlemek, damar duvarının içini iyileştirmek ve son olarak bozularak absorbe olmak üzere tasarlanmıştır. Çalışma, koyun ve domuzda fonksiyonel implantasyondan sonra veri toplamak ve analiz etmek, implantın dolaşım sisteminde kullanıldığında fizyolojik fonksiyonu sürdürme kapasitesini değerlendirmek, konakçının yanıtını ve cihazın tepkisini belirlemek (fiziksel bütünlük, feda edilme sırasında dokusal kapsülleme) ve implantın degradasyonunu değerlendirmek için tasarlanmıştır | 14 kapatma elemanı<br><br>2 koyuna implante edilen 8 kapatma elemanı,<br><br>1 domuza implante edilen 2 kapatma elemanı<br><br>Aynı femoral artere iki kapatma elemanı implante edildiğinde, 30 mm'den daha fazla bir mesafede implante edildiler | Dahili disk kapsüllemesine özel bir önem gösterilerek cihazın ilk dokusal entegrasyonuna özel dikkat gösterilmiştir.<br><br>Makroskopik olarak lokal intolerans veya tromboz oluşumuna dair önemli belirtiler gözlenmemiştir. Makroskopik gözlemede, femoral arterlerde kapatma elemanlarının implantasyonundan sonra koyun veya domuz arasında herhangi bir fark görülmemiştir. Makroskopik olarak lokal intolerans veya tromboz oluşumuna dair önemli belirtiler gözlenmemiştir. Makroskopik gözlemede, femoral arterlerde kapatma elemanlarının implantasyonundan sonra koyun veya domuz arasında herhangi bir fark görülmemiştir.<br><br>Koyunlarda implantasyon yerinin histopatolojik analizinde lokal advers reaksiyon görülmemiştir. İç ve dış diskler degradasyon belirtileri göstermiştir ve bazı durumlarda daha küçük parçalara bölünmüştür. İç diskler tamamen neointimal dokuya entegre edilmiştir. Domuzda histopatolojik analiz, iç ve dış disklerin etrafında biraz daha fazla enflamatuvar işaret göstermiştir. Her iki hayvanda da multifilaman, disk materyaline göre biraz daha fazla enflamatuvar belirti göstermiştir; bu da |
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| <b>İnsanlarda İlk Klinik Çalışma</b>                                                                                                                                                                         |                              |                                                  |                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| <b>Çalışma Başlığı</b>                                                                                                                                                                                       | <b>Yıl / CI</b>              | <b>Çalışma Türü</b>                              | <b>Amaçlar</b>                                                                                                                                                                                                                                                                                  | <b>Önemli Olaylar</b>                                                                                                                                                                                                                                                                                                                                            | <b>Potansiyel Kabul Edilme Kriterleri</b>                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Açık etiketli, tek kollu, çok merkezli araştırma | Çalışmanın amaçları, genel olarak FemoSeal Vascular Closure System (FemoSeal System) ve özellikle de kardiyak tanı veya girişimsel kardiyoloji prosedürlerinden femoral arter erişimi kullanılarak geçen hastalarda Kapatma Ögelerinin güvenliğini, performansını ve etkinliğini belirlemektir. | <p>2 bölümlü çalışma</p> <p>Toplam n = 80</p> <p>Bölüm 1 n = 20</p> <p>Bölüm 2 n = 60</p> <p>Endikasyonlar:</p> <p>Bölüm 1 - erişim alanı olarak femoral arter kullanılarak tanısal kardiyak kateterizasyon</p> <p>Bölüm 2 - erişim alanı olarak femoral arter kullanarak tanısal ve girişimsel kardiyak prosedürler geçiren hastalar</p> <p>30 günlük takip</p> | <p>Sonuçlar</p> <p><u>-sıkıştırma olmadan FS ile elde edilen hemostaz</u></p> <p>- Bölüm 1 20/20 (%100)</p> <p>- Bölüm 2 58/60 (%97)</p> <p>Prosedür sırasında hemostaz için medyan süre (bölüm 2) - 1,0 dakika (Anında aralık - 8 dakika)</p> <p><u>Ambülasyon süresi (dakika)</u></p> <p>Bölüm 1 - Medyan: 33,0 ortalama: 67,8</p> <p>Bölüm 2 - medyan: 45 ortalama: 87,5</p> <p><u>Önemli vasküler komplikasyonların insidansı - 30 günlük takip</u></p>            |

|  |  |  |  |  | <p>Bölüm 1<br/>-Vasküler komplikasyon<br/>yok 20/20 (%100)</p> <p>Bölüm 2<br/>Psödoanevrizma - 1/59<br/>(%1,69)</p> <p><u>Tedavinin başarısız<br/>olması</u><br/>Bölüm 1 - 0/20 (%0)<br/>Bölüm 2 - 3/60 (%5)<br/>• 2 Kompresyon<br/>kullanılmadan<br/>hemostaz elde<br/>edilememesi<br/>nedeniyle<br/>• 1 önemli vasküler<br/>komplikasyona bağlı<br/>olarak,<br/>psödoanevrizma</p> <p><u>Kalıcı sızma</u><br/>Bölüm 1 - 0/20 (%0)<br/>Bölüm 2 - 8/60 (%13)</p> <p><u>Hematom</u><br/>Bölüm 1 - 0/20 (%0)<br/>Bölüm 2 - 6/60 (%10)</p> |
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FemoSeal™ VCS için pazarlama öncesi geliştirme planının bir parçası olarak 3 hayvan fonksiyonel testi tamamlanmıştır. 2000 yılında, klinik çalışmalara başlamadan önce FemoSeal™ VCS'nin biyoişlevselliğini değerlendirmek için bir hayvan çalışması yapılmıştır. Bu çalışma, fizyolojik fonksiyonu korumak ve degradasyonlarını değerlendirmek için kapatma unsurlarının kapasitesini değerlendirmiştir. 18. ayda, iç ve dış disk materyali endolüminal fibröz doku ile değiştirildiği için artık görünmüyordu. Sonuç olarak, dolaşım sisteminde kullanıldığında FemoSeal™ VCS kapatma elemanının fizyolojik işlevini sürdürebilmesi onaylanmıştır.

2002 yılında, vasküler sistemde hemostaz elde etmek için tasarlanmış biyolojik olarak parçalanabilen bir implant olan FemoSeal™ VCS'nin biyoyumluluğunu ve biyoişlevselliğini değerlendirmek için bir hayvan çalışması yapılmıştır. Özetle, implantın degradasyonu yaklaşık 36 hafta önce tamamlanmış ve önemli bir advers dokusal reaksiyon görülmemiştir.

2002 yılında yapılan bir başka hayvan çalışması, vasküler sistemde hemostaz elde etmek için tasarlanmış biyolojik olarak parçalanabilen bir implant olan FemoSeal™ VCS'nin biyouyumluluğunu ve biyoışlevselliğini değerlendirdi. 5 hafta sonra diskin kapsüllenmesi tamamlandı ve iç ve dış disklerde degradasyon izleri gözlemlendi. Sonuç olarak, dolaşım sisteminde kullanıldığında implantın fizyolojik fonksiyonunu sürdürme kapasitesi onaylanmıştır.

FemoSeal™ VCS için klinik geliştirme planının bir parçası olarak, Radi Medical System AB pazar öncesi bir klinik araştırma gerçekleştirmiştir. Bu klinik araştırma yayınlanmamıştır veya çevrimiçi olarak sunulmamaktadır. 11200 numaralı cihaz modeli ile yapılan çalışma, 2002-2004 yıllarında Avrupa Standardı EN 540 (İnsan Denekler için Tıbbi Cihazların Klinik Araştırması) kapsamında ve ICH Klinik Araştırmalar için Genel Hususlar ve İyi Klinik Uygulama Kılavuzu'na uygun olarak gerçekleştirilmiştir. Bu çalışmanın ayrıntıları EU-SE-001 raporunda belgelenmiştir. Bu klinik araştırma, Radi Medical Systems AB'nin "Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures" isimli çalışmasının Nihai Raporunda belgelenmiştir. Söz konusu klinik çalışma, FemoSeal™'ın 11200 numaralı ilk modeliyle gerçekleştirilmiş ve implante edilebilir kapatma bileşenlerinin güvenliliğine ve etkililiğine odaklanmıştır. İlk model 11200 ile mevcut model C11202 arasındaki tek fark, sırasıyla 6F ve 7F French boyutu ve geliştirilmiş uygulama sistemidir. İmplant edilebilir kapatma elemanlarının, iç kapağın ve dış kilitleme diskinin klinik faydaları, kullanım amacı, çalışma ilkeleri ve ham maddeleri değişmeden kalır.

Cihazın kullanım amacı, femoral arteri erişim noktası olarak kullanarak tanısal kardiyak veya girişimsel kardiyak prosedürler uygulanan hastalar içindir. Bu çalışmanın amacı, FemoSeal™ VCS'nin güvenliğini, performansını ve etkililiğini belirlemektir. Bu çalışma, 30 günlük takip ile ileriye dönük, çok merkezli, tek kollu, açık etiketli bir çalışmaydı.

Birincil performans sonlanım noktası, akut kanamanın olmaması olarak tanımlanan hemostaz süresiydi. Birincil güvenlik sonlanım noktası, 30 gün içinde önemli vasküler komplikasyonların görülme sıklığıydı. İkincil sonlanım noktaları arasında ambülasyona kadar geçen süre, tedavi başarısızlıklarının oranı, advers olayların görülme sıklığı ve uygulama ve yerleştirme sırasında cihaz performans özellikleri yer aldı.

Bu çalışmaya dahil edilen hastalar, bilgilendirilmiş onam verebilen ve en az bir sağlam pedal pulsatifi olan yetişkinlerdi. Hastalar aşağıdaki durumlardan herhangi birine sahipse çalışma dışı bırakılmıştır:

- Periferik vasküler hastalık öyküsü
- Otoimmün hastalık
- Şiddetli anemide bilinen kanama bozukluğu
- INR >1,5

- 72 saat içinde miyokard enfarktüsü
- Tedaviye rağmen kontrolsüz hipertansiyon
- Seldinger tekniği ile erişimi engelleyen obezite
- Arteriyotomi bölgesinde vasküler greft veya stent varlığı
- 3 ay içinde önceki ipsilateral ponksiyon
- Kullanım ömrü < 6 ay

Ek olarak, hastalar intraoperatif olarak muayene edilmiştir ve aşağıdakilerden herhangi biri gözlemlenirse çalışmadan hariç tutulmuştur:

- Ortak femoral arterin lümen çapı <5 mm
- Ponksiyon bölgesine 2 cm proksimal arteriyel dallar
- Ponksiyon bölgesinin 3 cm içinde belirgin stenoz
- Birincil giriş seti kılıfının kullanımı >6Fr
- Femuoral bifürkasyonunda veya distalinde ponksiyon
- Çoklu femoral ponksiyonlar
- Bilinen veya şüphelenilen posterior femoral duvar ponksiyonu
- Prosedürün tamamlanmasından sonra büyük hematoma (2:6 cm)
- Kıvrık doku veya damar nedeniyle prosedür için zor birincil kılıf yerleştirilmesi

Bu tek protokol çalışması iki bölümde gerçekleştirilmiştir: Bölüm 1'de 20 hasta kaydedilmiş, ardından bir güvenlik analizi tamamlanmıştır ve ardından Bölüm 2'de 60 hasta daha kaydedilmiştir.

Bölüm 1'de, kayıtlı hastaların ortalama yaşı 65,9'du, hastaların %70,0'u erkekti ve %95'i eş zamanlı olarak ilaç kullanmaktaydı. Çalışmanın 2. bölümünde ortalama yaş 63,8'di, %78'i erkekti ve %100'ü eş zamanlı olarak ilaç kullanmaktaydı.

Tanısal (Bölüm 1 ve Bölüm 2) veya girişimsel (Bölüm 2) kardiyak kateterizasyon işlemleri yapılan hastalar çalışmaya kaydolmak için uygun görülmüştür. FemoSeal™ VCS kullanıldıktan sonra prosedürler, kaydolan hastanelerin her birinde bakım standardıyla uyumluydu. Hasta verileri başlangıçta, prosedür sırasında ve prosedürden 1 gün sonra ve 30 gün sonra toplanmıştır. Sonuçlar **Tablo 1.5'te** özetlenmiştir ve FemoSeal™ VCS'nin bu hasta popülasyonunda kullanım için güvenli ve etkili olduğunu göstermektedir.



**Tablo 1.5 Pazarlama Öncesi Çalışmada Rapor Edilen Klinik Sonuçlar**

|                                                                                                                                       | <b>Bölüm 1</b> | <b>Bölüm 2</b>           |
|---------------------------------------------------------------------------------------------------------------------------------------|----------------|--------------------------|
| Hasta sayısı                                                                                                                          | 20             | 60                       |
| Ortalama Hemostaz Süresi                                                                                                              | 1,2 dakika     | 1,6 dakika <sup>a</sup>  |
| Ortalama Ambülasyon Süresi                                                                                                            | 72,2 dakika    | 87,5 dakika <sup>b</sup> |
| Önemli Vasküler<br>Komplikasyonların İnsidansı <sup>c</sup>                                                                           | 0 (%0)         | 1 (%2)                   |
| Advers Olay Görülen Hasta<br>Sayısı                                                                                                   | 5 (%25)        | 19 (%32)                 |
| Tedavinin başarısız olması<br>(önemli vasküler<br>komplikasyonlar, manuel<br>kompresyon ihtiyacı veya her<br>ikisi olarak tanımlanır) | 0 (%0)         | 3 (%5)                   |
| Cihaz Arızaları                                                                                                                       | 0 (%0)         | 6 (%10)                  |

<sup>a</sup> Toplam örneklem büyüklüğü 58 olarak hesaplanmıştır, çünkü 2 hasta önceki ipsilateral ponksiyonlar nedeniyle işlem sırasında hemostaza ulaşmamıştır. Bu hastalarda 7 dakikada ve 37 dakikada hemostaz sağlandı.

<sup>b</sup> Toplam 59 örneklem büyüklüğüne dayalı olarak: 1 hasta pulmoner ödem nedeniyle ventilatöre yerleştirildiği ve bir haftadan fazla ambülasyon yapamadığı için çalışmaya dahil edilmemiştir.

<sup>c</sup> Kan transfüzyonu veya cerrahi onarım gerektiren vasküler komplikasyon veya antibiyotik uygulanması, hastaneye yatış veya hastaneye yatış uzatma veya bölge debridmanı gerektiren lokal enfeksiyon olarak tanımlanır

Çalışmanın 1. bölümünde önemli vasküler komplikasyonlar gözlenmemiştir. Çalışmanın 2. Bölümünde bildirilen 1 majör vasküler komplikasyon bulunmaktadır: prosedürden 1 gün sonra bildirilen psödoanevrizma. Olay, ultrason eşliğinde kompresyon ve psödoanevrizmaya trombin enjeksiyonu gerektirmiştir ve hastanın hastanede yatış süresini uzatmıştır.

Çalışmanın 1. Bölümünde bildirilen 5 advers olay arasından 1 advers olay muhtemelen cihazla ilgiliydi: prosedürden 1 gün sonra ciddi olmayan bir akut kanama olayı. Çalışmanın 2. Bölümünde bildirilen 19 advers olay arasından cihazla ilişkili ciddi olmayan 3 advers hematoma olayı gözlemlendi ve 3 adet kalıcı sızma, 2 adet hematoma ve 1 adet egzersiz sonrası bacak ağrısı bildirimi dâhil olmak üzere muhtemelen cihazla ilgili ciddi olmayan 6 adet olay gözlemlendi.

2. Bölümde tedavisi başarısız olarak kabul edilen 3 hasta vardı: 2'si kompresyon kullanılmadan hemostaz elde edilememesi nedeniyle ve 1'i majör vasküler komplikasyon (psödoanevrizma) nedeniyle. Çalışmanın 1. Bölümünde başarısız tedavi görülmemiştir.

Çalışmanın 2. Bölümündeki altı cihaz arızasından üçü prosedüre müdahale etmedi, biri kullanıcı hatasına atfedildi, biri giriş setinden kaynaklanan bir sızıntıydı ve biri de kırık bir filament eklemiydi. Son iki sorun C11202'de uygulanmış olan model güncellemeleri ile giderilmiştir.

Pazar öncesi klinik çalışmanın 2. Bölümü, hastanın uyumsuzluğundan kaynaklanan 6 aylık takip sonuçlarını rapor etmemiştir. Klinik literatürün takip süresiyle uyumlu olan pazar öncesi klinik çalışma (EU-SE-001) 30 günlük sonuçları, FemoSeal™ VCS'in güvenli ve etkili olduğunu göstermektedir.

#### 1.4.2 Pazarlama Sonrası Klinik Çalışmalardan Elde Edilen Verilerin Özeti

Aşağıdaki **Tablo 1.6**'da açıklanan, tamamlanmış 4 adet pazarlama sonrası klinik çalışma bulunmaktadır. Bu klinik araştırmalar yayınlanmamıştır veya çevrimiçi olarak sunulmamaktadır.

**Tablo 1.6 Pazarlama Sonrası Klinik Çalışmalar**

| Pazarlama Sonrası Tamamlanan Klinik Çalışmalar                                              |                                                             |                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                              |
|---------------------------------------------------------------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Çalışma Başlığı                                                                             | Yıl / CI                                                    | Çalışma Türü                                                                  | Amaçlar                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Önemli Olaylar                                                                                                                                                                                                                                                           | Potansiyel Kabul Edilme Kriterleri                                                                                                                                                                                                                                                                           |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI                                                | Pazar Sonrası Çalışma, Yeni Paketin Kullanıcı Tarafından Kabul Edilebilirliği | İşlevselliği belgelemek için ilk model 11200'e kıyasla değiştirilmiş bir uygulama sistemine sahip olan FemoSeal Vascular® Closure System 11202 model güncellemesi üzerinde yapılan pazar sonrası çalışma.<br>Çalışmanın amacı doktorlar ve hemşireler için eğitim projesi olan revize edilmiş Kullanım Talimatları (IFU) hakkında geri bildirim almak, risk analizinde yapılan değerlendirmeleri onaylamak ve herhangi bir ürün kalitesi iyileştirmesine girdi sağlamaktır. | 100 hasta<br>• 63 erkek / 37 kadın<br>• Kadınların yaş ortalaması 68, erkeklerin yaş ortalaması 65<br>2 İsveç hastanesi, 6 doktor<br>112 cihaz<br>Hasta kayıt formlarından (CRF) elde edilen veriler<br>Planlanan gözlem süresi - uygulama zamanından itibaren 30 dakika | Sonuçlar<br>1. Kullanma Talimatlarındaki resimler/talimatlar bilgilendirici ve yeterli kabul edilmiştir<br>2. Anında hemostaz (91/100)                                                                                                                                                                       |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)           | Dr. Nicolas Moes<br>Innsbruck Medical University, Avusturya | Pazar Sonrası Doğrulayıcı Değerlendirme                                       | Bu çalışmanın amacı, tanısal kardiyak kateterizasyon veya 7F kılıf ile gerçekleştirilen perkütan kardiyak girişimsel prosedür uygulanan hastalarda normal klinik rutin sırasında kullanılan FemoSeal®'in güvenliğini ve performansını değerlendirmektir.                                                                                                                                                                                                                    | 50 ardışık hasta<br>Endikasyon - ortak femoral arterden tanısal veya invaziv kardiyak kateterizasyon                                                                                                                                                                     | Birincil sonlanım noktaları<br>• Birincil etkililik sonlanım noktası - TTH (hemostaz süresi) sızıntı olan veya sızıntı olmayan, ancak herhangi bir ek sıkıştırma olmadan, manuel veya mekanik.<br>• Güvenlik sonlanım noktası - advers olayların insidansı - küçük ve önemli vasküler komplikasyonlar ve tüm |

|                                                                                |            |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|--------------------------------------------------------------------------------|------------|-----------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----|-----|----------|-------|----------|-----------|----|-----------|-----------|-------------------------|----------|--------------------|------------|---------------------|-----------|-------------------|---------|-----------------------|----------|--------------------------------|----------|----------------------|-----------|--------------------------|-----------|-----------------------------------|----------|----------------------|--------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                |            |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | <table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.8±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.8±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | <p>diğer advers olaylar - çalışmanın süresi boyunca (yani hastanın taburcu olmasına kadar) ciddi olan ve ciddi olmayan olaylar.</p> <p><b>Sonuçlar</b></p> <ul style="list-style-type: none"><li>Ortalama Hemostaz Süresi</li><li>Tanı - 56,6 ± 29 saniye</li><li>Girişimsel 59,9 ± 16,2 saniye</li><li>Tüm hastalar 57,8 ±26,3</li><li>Tüm hastalar 4 saat yatak istirahadinden sonra sorunsuz bir şekilde ambüle edilebildi.</li></ul> <p><b>Güvenlik sonuçları</b></p> <ul style="list-style-type: none"><li>50 vakadan 49'u (%98) hastaneden taburcu olana kadar vasküler komplikasyon yaşamadı</li><li>Ortalama taburcu olma süresi 2,6 gün</li><li>50 vakadan 1'i (%2) anjiyografi gününde sorunsuz ambülasyon sonrası ertesi gün hafif kanama yaşadı</li></ul> |
| n                                                                              | 50         |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| men                                                                            | 35 (70%)   |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| women                                                                          | 15 (30%)   |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| PCI cases                                                                      | 15         |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| age (yrs)                                                                      | 62.8±11.1  |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| body mass index (kg/m²)                                                        | 25.4±6.7   |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| systolic BP (mmHg)                                                             | 131.2±20.9 |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| diastolic BP (mmHg)                                                            | 77.9±10.6  |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| diabetes mellitus                                                              | 9 (18%)    |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| arterial hypertension                                                          | 34 (68%)   |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| previous coronary intervention                                                 | 13 (26%)   |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| preprocedure aspirin                                                           | 50 (100%)  |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| preprocedure clopidogrel                                                       | 50 (100%)  |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Procedural unfractionated heparin                                              | 15 (30%)   |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Procedural abciximab                                                           | 2 (4%)     |                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009) | 2009 RADI  | Pazar Sonrası Çalışma | <p>Çalışma, müşterilerin/kullanıcıların yeni pakette, özellikle de Tuvek/PET-PE poşetin steril olmayan dış kısmında bir sorun tespit edip etmediklerini belirtmelidir.</p> <p>Çalışma ayrıca, tedaviyi gerçekleştiren doktorun cihazın uygulanma/yerleştirme adımlarında daha önce kullanılan cihazlara kıyasla herhangi bir fark görüp görmediği hakkında bilgi sağlamalıdır.</p> <p>Çalışma ayrıca ürün kalitesini iyileştirmeye yönelik diğer tüm ihtiyaçlara dair bilgi sağlayacaktır.</p> | <p>25 adet cihaz</p> <p>4 İsveç hastanesi</p> <p>Hastaların 16/25'i (%64), antikoagülasyon ilaçları ağır olan PCI hastalarıydı</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <p><b>Sonuçlar</b></p> <ol style="list-style-type: none"><li>Paketle ilgili sorunlar – 25 uygulamanın 21'inde (%84) başarılı oldu; 4'ünde (%16) başarısız oldu (1 - yeni giriş setinin test edilmesi, 1 iç diskin destek basamağında arteriyotomiden geçirilmesi, düğmenin yukarı çıkması ve dış diskin insizyon doku kanalına yerleştirilmesi, 2 acil hemostaz yapılmamasına rağmen yerleştirme sorunu yaşanmadı.)</li><li>Anında hemostaz, 25 hastanın 19'u (%76)</li><li>Kanama 25 hastanın 11'inde (%44) – 25 hastanın 9'unda (%36) sızıntı/kanama, 25 hastanın 2'sinde (%8) hematom</li></ol> <p>Toplam olay oranı %19</p> |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |

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| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022) | 2022/ Terumo Medical Corporation | Prospektif, Çok merkezli, Gözlemsel, Pazarlama sonrası | FemoSeal™ VCS'nin perkütan endovasküler prosedürler uygulanan gerçek dünya gönüllülerinde ortak femoral arter (CFA) erişim bölgelerinin hemostazının elde edilmesinde güvenliliğini ve etkililiğini daha da fazla göstermek | <ul style="list-style-type: none"> <li>Hastane ziyareti veya telefon görüşmesi yoluyla 30. günde (<math>\pm 7</math> gün) hasta takibi.</li> <li>Kayıt: Aralık 2021'den Temmuz 2022'ye kadar.</li> <li>FemoSeal™'in kullanıldığı tanısal veya girişimsel endovasküler prosedürler uygulanan kayıtlı 230 gönüllü.</li> </ul> <p>3 Avrupa merkezi: Fransa (92 hasta), Almanya (38 hasta), Belçika (100 hasta).</p> | <ul style="list-style-type: none"> <li><b>Demografi/ komorbiditeler:</b> <ul style="list-style-type: none"> <li>Cinsiyet: 161 erkek (%70)/69 kadın (%30).</li> <li>Ortalama yaş: <math>70 \pm 12</math>.</li> <li>VKİ: <math>26,1 \pm 4,95</math> kg/m<sup>2</sup>.</li> <li>Hipertansiyon: 160 hasta (%69,6).</li> <li>Dislipidemi: 128 (%55,7).</li> <li>Koroner arter hastalığı: 42 (%18,3).</li> <li>Şu anda sigara içen: 86 (%37,6).</li> <li>Geçmişte sigara içen: 66 (%28,8).</li> <li>Koroner kalp hastalığı: 34 (%14).</li> <li>Önceki miyokard enfarktüsü: 18 (%7,8).</li> <li>Periferik arter revaskülarizasyonu: 12 (%5,2) karotid ve 83 (%37,5) alt ekstremitte arteri.</li> <li>Antiplaletet tedavisi (başlangıçta): 21 (%9,1) ikili antiplatelet tedavisi (DAPT) dâhil olmak üzere 211 (%91,7).</li> <li>Oral antikoagülasyon: 40 (%17,4) hasta.</li> </ul> </li> <li><b>Müdahale özellikleri:</b> <ul style="list-style-type: none"> <li>Ortam: yatarak tedavi kliniğinde 162 vaka (%70,4), poliklinikte 68 vaka (%29,6).</li> <li>Yaygın endikasyon: klodikasyon 147 vaka (%63,9).</li> <li>Yaklaşım: 35 antegrad (%15,3), 194 retrograd (%84,7).</li> </ul> </li> <li><b>Birincil Sonlanım Noktaları:</b> <ul style="list-style-type: none"> <li>Tam Analiz Kümesi'ndeki 215/226 (%95,1) [%95 CI: 91,46; 97,55] hastada ve FemoSeal™ ile Tedavi Kümesi'ndeki 215/230 (%93,5) [%95 CI: 89,47,</li> </ul> </li> </ul> |
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|  |  |  |  |  | <p>96,30] hastada birleşik güvenlik (prosedürden sonraki 6 saat içinde erişim bölgesi ekstremitesinde majör komplikasyonlar olmaması) ve etkililik (başarılı ponksiyon bölgesi hemostazı) sonlanım noktasına ulaşılmıştır.</p> <p>- Hastaların 219/226'sında (%96,9) [CI: 93,7, 98,7] etkililik sonlanım noktasına ulaşılmıştır.</p> <p>- 220/230 (%95,2) [%95 CI: 92,15, 97,90] hastada güvenlik sonlanım noktasına ulaşılmıştır.</p> <p>• <b>İkincil sonlanım noktaları:</b></p> <p>- 225/230 (%97,8) [%95 CI: 95,00; 99,29] hastada prosedürden sonraki altı saat boyunca minör erişim bölgesi komplikasyonları olmamıştır.</p> <p>- Hastaların 219/230'unda (%95,2) [%95 CI: 91,60; 97,59], prosedürden sonra altıncı saatten 30. güne kadar majör ve minör erişim bölgesi komplikasyonları olmamıştır.</p> <p>- FemoSeal™ VCD ile medyan hemostaz süresi: 0,42 (0,25; 0,50) dakika.</p> <p>- Medyan ambülasyon süresi: 5,00 (4,54; 5,50) dakika.</p> <p>- Medyan hastanede kalış süresi: 23,98 (22,72, 25,00) saat.</p> <p>- FemoSeal™ VCS'nin kullanılabilirliği: vakaların %98,7'sinde yerleştirilmesi "kolay" veya "çok kolay" (21 vakada yerleştirilmesi "kolay" (%9,2), 205</p> |
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|  |  |  |  |  | <p>vakada yerleştirilmesi "çok kolay" (%89,5)), vakaların 226'sında yerleştirme sırasında direnç yok veya düşük (%98,3).</p> <p>Hastaların 152/230'u (%66,1) FemoSeal™ kiti (GW 0,038") ile birlikte verilen kılavuz tel kullanılarak tedavi edildi ve herhangi bir cihaz eksikliği veya advers olay bildirilmeden FemoSeal™ tavsiye edildi.</p> |
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2006 çalışması, geliştirilmiş uygulama cihazı ile mevcut cihazın güvenliğini ve etkililiğini doğrulamak ve FemoSeal™ VCS Kullanım Talimatı ve eğitim programı hakkında geri bildirim almak için yapılmıştır. Çalışmaya 100 hasta dahil edilmiştir ve birincil sonlanım noktası hemostaz sağlanıp sağlanmadığı veya ek manuel veya mekanik kompresyonlara ihtiyaç duyulup duyulmadığıydı. Bu çalışma FemoSeal™ VCS uygulamasının vakaların çoğunda başarılı olduğu sonucuna varmıştır (%91'inde anında hemostaz sağlamıştır).

2008 çalışmasına, 7 Fr kılıfıyla kardiyak kateterizasyon uygulanan hastalarda normal klinik rutin sırasında kullanıldığında FemoSeal™ VCS'nin güvenlik ve performansını değerlendirmek için 50 hasta alındı. Çalışmanın birincil sonlanım noktası hemostaz süresi ve ek kompresyon, manuel veya mekanik olmadan ambülasyon süresi ile ilgili veri toplamaktır. Çalışma sonuçlarına göre, ortalama hemostaz süresinin 57,8 saniye olduğu ve tüm hastaların 4 saat yatak istirahatinden sonra ambüle olduğuna ulaşılmıştır.

2009 yılında yapılan çalışma yeni FemoSeal™ VCS ambalajını değerlendirmek için yapılmıştır. Çalışmaya 25 hasta alınmıştır. Birincil sonlanım noktası, kullanıcının paketle ilgili herhangi bir sorun yaşayıp yaşamadığıydı. Kullanıcılar yeni FemoSeal™ VCS paketiyle ilgili herhangi bir sorun görmedi. Bu çalışma ile aynı zamanda hemostaz süresi için de veri toplamıştır.

2022 tarihinde yapılan çalışmanın amacı, FemoSeal VCS'nin perkütan endovasküler prosedürler uygulanan gerçek dünya gönüllülerinde ortak femoral arter (CFA) erişim bölgelerinin hemostazının elde edilmesinde güvenliliğine ve etkililiğine dair verileri proaktif olarak toplamaktır. Çalışmaya 230 hasta alınmıştır. Kayıt için birincil sonlanım noktaları prosedürel başarı (yani başarılı ponksiyon bölgesi hemostazı) ve majör komplikasyonlarda azalmadır (örneğin, vasküler yaralanma, erişim bölgesi ile ilgili kanama, erişim bölgesi enfeksiyonu, tekrarlayan manuel kompresyon ve yeni erişim bölgesi ile ilişkili ipsilateral akut bacak iskemisi). Çalışma, FemoSeal™ VCS'nin gerçek dünya ortamlarında iyi performans gösterdiği ve periferik endovasküler müdahaleler uygulanan hastalarda etkili hemostaz ve düşük erişim bölgesi komplikasyon oranları sağladığı sonucuna varmıştır. FemoSeal™ VCS, kısa hemostaz süresi ve

iyi operatör kullanılabilirlik geri bildirimleri ile iyi bir performans sergilemektedir; bu da onu femoral erişim kapatma açısından değerli bir cihaz hâline getirmektedir.

### 1.4.3 Pazarlama Sonrası Klinik Takipten Elde Edilen Verilerin Özeti

#### 1.4.3.1 Tamamlanan Pazarlama Sonrası Klinik Takip

Tamamlanan pazarlama sonrası klinik takip faaliyetlerinin bir özeti, aşağıdaki **Tablo 1.7'de** açıklanmıştır.

**Tablo 1.7. Pazar Sonrası Klinik Takip Faaliyetleri**

| Tamamlanan Pazarlama Sonrası Klinik Takip Faaliyetleri                    |          |                                                                |                                                                                                                                                                               |                                                                                                                                                                                                                                                                                               | Potansiyel Kabul Edilme Kriterleri                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|---------------------------------------------------------------------------|----------|----------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Faaliyet Adı                                                              | Yıl/CI   | Çalışma Türü                                                   | Amaçlar                                                                                                                                                                       | Önemli Olaylar                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021 TMC | Pazarlama Sonrası Klinik Araştırma - yüksek kaliteli araştırma | Avrupa Birliği pazarlarında dağıtımı yapılan FemoSeal™ Vascular Closure Device'in kullanımına ilişkin potansiyel geri bildirimleri toplamak için pazarlama sonrası araştırma. | <ul style="list-style-type: none"><li>120 vaka</li><li>5 yıldan fazla deneyime sahip 8 farklı doktor</li><li>Avrupa'da birden fazla ülke</li></ul>                                                                                                                                            | <b>1-5 üzerinden cihaz değerlendirmeleri - Araştırma bildirimleri</b> <ul style="list-style-type: none"><li>Kabul kriterleri<ul style="list-style-type: none"><li>3-5 arasındaki değerlendirmeler olumlu kabul edilir</li><li>Tüm bildirimler ≥ %80 olumlu geri bildirim içermelidir</li></ul></li><li>Sonuçlar<ul style="list-style-type: none"><li>Hiçbir araştırma bildiriminde &gt; %20 olumsuz yanıt alınmamıştır</li><li>Ürünle ilgili hiçbir şikâyet doldurulmamıştır</li></ul></li></ul> |
| 20210298 – 0.035” and 0038” Guidewire Clinical Survey Report (2021)       | 2021 TMC | Pazarlama Sonrası Klinik Araştırma - yüksek kaliteli araştırma | Avrupa Birliği pazarlarında dağıtımı yapılan 6Fr Angio-Seal™ VIP Vascular Closure Device (VCD) ile birlikte verilen 0,035 inç kılavuz tel ve 8Fr Angio-Seal™ VIP              | <ul style="list-style-type: none"><li>0,035 inç tele yönelik araştırmalar<ul style="list-style-type: none"><li>106 araştırma</li><li>64 doktor</li></ul></li><li>0,038 inç tele yönelik araştırmalar<ul style="list-style-type: none"><li>109 araştırma</li><li>55 doktor</li></ul></li></ul> | <b>1-5 üzerinden cihaz değerlendirmeleri - Araştırma bildirimleri</b> <ul style="list-style-type: none"><li>Kabul kriterleri<ul style="list-style-type: none"><li>3-5 arasındaki değerlendirmeler olumlu kabul edilir</li><li>Tüm bildirimler ≥ %80 olumlu geri bildirim içermelidir</li></ul></li><li>Sonuçlar</li></ul>                                                                                                                                                                        |

| Tamamlanan Pazarlama Sonrası Klinik Takip Faaliyetleri                                                                          |                     |                                                                |                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|---------------------------------------------------------------------------------------------------------------------------------|---------------------|----------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                 |                     |                                                                | VCD ve FemoSeal Vascular Closure System ile birlikte verilen 0,038 inç kılavuz telin kullanımına ilişkin potansiyel geri bildirimleri toplamak için pazarlama sonrası araştırma. | <ul style="list-style-type: none"><li>12 geriye dönük araştırma</li></ul>                                                                                                                                                                                                                  | <ul style="list-style-type: none"><li>Tüm kılavuz teller kabul edilebilir derecelendirmeleri almıştır</li><li>Ürünle ilgili hiçbir şikâyet doldurulmamıştır</li></ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023-2024<br>TMC/TE | Pazarlama Sonrası Klinik Araştırma - yüksek kaliteli araştırma | FemoSeal VCS'nin AB pazarında dağıtılan kılavuz teller ile kullanımına ilişkin potansiyel olarak geri bildirim toplamak için.                                                    | <ul style="list-style-type: none"><li>126 Araştırma</li><li>7 merkez</li><li>5 ülke</li><li>14 Kasım 2023-11 Haziran 2024</li><li>Doktorun tıbbi uzmanlık alanı:<ul style="list-style-type: none"><li>Vasküler cerrahi</li><li>Girişimsel radyoloji</li><li>Anjiyoloji</li></ul></li></ul> | <b>5 üzerinden cihaz değerlendirmeleri - Araştırma bildirimleri</b> <ul style="list-style-type: none"><li>Kabul kriterleri<ul style="list-style-type: none"><li>3-5 arasındaki değerlendirmeler olumlu kabul edilir</li><li>Tüm bildirimler ≥ %80 olumlu geri bildirim içermelidir</li><li>Bu araştırmada advers olaylar meydana gelirse bu olaylar risk yönetimi tarafından öngörülenler olmalıdır.</li></ul></li><li>Hasta Demografisi<ul style="list-style-type: none"><li>Kadın: %29,4 (37/126)</li><li>Erkek: %69,8 (88/126)</li><li>Açıklanmayan cinsiyet: 0,8 (1/126)</li><li>Yaş &gt;75 yaş: %31,7</li></ul></li><li>Sonuçlar<ul style="list-style-type: none"><li>FemoSeal™ VCS ile birlikte verilen</li></ul></li></ul> |



| Tamamlanan Pazarlama Sonrası Klinik Takip Faaliyetleri |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|--------------------------------------------------------|--|--|--|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                        |  |  |  |  | <p>kılavuz tel:<br/>101/126 (%80,2).</p> <ul style="list-style-type: none"><li>○ Prosedür süresi (dakika): 63,4 (36,6) [ortalama (SD)]; 57,0 (36,0-81,0) [Medyan (IQR)]</li><li>○ Tüm FemoSeal™ VCS performans derecelendirmeleri olumluydu.</li><li>○ FemoSeal™ VCS tarafından sağlanan tüm kılavuz tel derecelendirmeleri olumluydu.</li><li>○ Bir (%0,8) advers olay: FemoSeal™ VCS diskleri muhtemelen hemostaz sağlamak için manuel kompresyon gerektiren sert bir kılavuz telin (Boston Scientific Amplatz Super Stiff, 75 cm, 0,035 inç) kullanılması nedeniyle iyi hızalanmamıştır.</li></ul> |

Terumo Medical Corporation, mevcut raporlama döneminde (1 Eylül 2019-31 Ağustos 2024) üç tane yüksek kaliteli doktor kullanıcı araştırması tamamladı.

FemoSeal™ Klinik Araştırmaları, klinik kullanım sırasında FemoSeal™ VCS'nin güvenliği ve performansı ile ilgili proaktif klinik verileri toplamıştır. Araştırma, 0,038 inç kılavuz tel dahil olmak üzere genel cihaza ve ilgili aksesuarlara ve bunların doğrudan etkileşimlerine odaklanan sorular içeriyordu. Kılavuz tel klinik araştırmaları, FemoSeal™ VCS ile birlikte verilen 0,038 inç kılavuz telin klinik kullanımı sırasında güvenlik ve performansla ilgili proaktif klinik verileri toplamıştır. Araştırma soruları, kılavuz telin çıkarılmasıyla, prosedür kılıfının vaskülatüre yerleştirilmesinden başlayıp, kılavuz telin genel kullanımına odaklanmıştır.

Cihazla birlikte verilen FemoSeal™ VCS ve 0,038 inç kılavuz tel, tüm kabul edilebilir derecelendirmeleri almıştır ve yüksek kaliteli klinik araştırmalardan alınan yorumların değerlendirilmesine dayanarak cihaz için altı (6) şikâyet ve kılavuz tel için dokuz (9) şikâyet kaydedilmiştir. Şikâyetler hem FemoSeal hem de kılavuz tel için değerlendirmeye tabi tutulmuştur ve Terumo pazarlama sonrası gözetim sürecinin bir parçası olarak değerlendirilmiştir. Tanımlanan yeni bir risk ve/veya risk seviyesi yoktu.

PMCF faaliyetlerinin bir parçası olarak 2024 yılında bir doktor kullanıcı araştırması tamamlandı. Araştırma sonuçları, FemoSeal™ VCS performans derecelendirmesinin ve güvenliğinin genel olarak oldukça olumlu olduğunu göstermiştir. FemoSeal™ VCS ile birlikte sağlanan standart telin dışındaki kılavuz tellerin uyumluluğu da gösterilmiştir.

#### 1.4.3.2 Devam Eden/Planlanan Pazarlama Sonrası Klinik Takip

TMC'nin devam eden/planlanan bir adet pazarlama sonrası klinik takip faaliyeti vardır. FemoSeal VCS'nin AB pazarında dağıtılması ile kılavuz telin kullanımıyla ilgili prospektif olarak geri bildirim toplamak için bir klinik araştırma yapılacaktır. Araştırma, doktorlar tarafından prosedür sırasında hangi kılavuz telleri kullandıklarını araştırmak için tamamlanacaktır. Bu araştırmanın amacı, FemoSeal™ VCS'nin Terumo dışındaki markalara ait diğer kılavuz tellerin kullanımı ile uyumluluğu hakkında literatür ve haricî inceleyci yorumu eksikliği olarak tanımlanan bir boşluğu ele almaktır. Geri bildirim, cihazın farklı kılavuz tellerle performansı ile ilgili teknik sonuçları, klinik performansı ve güvenliği içerir.

#### 1.4.4 Sistematik Literatür İncelemesinden Elde Edilen Verilerin Özeti

Terumo Medical Corporation, FemoSeal™ VCS ve/veya benzer cihazlar hakkında yayımlanan çalışmalardan elde edilen klinik güvenilirlik ve performans verilerini toplamak ve değerlendirmek için sistematik literatür taramaları gerçekleştirmektedir. Yayımlanan literatürün yıllık olarak taranmasının amacı; daha önce bilinmeyen yan etkileri tanımlamak, bilinen yan etkileri izlemek, ortaya çıkan riskleri belirlemek ve FemoSeal™ VCS'nin olası sistematik yanlış kullanımını veya etiket dışı kullanımını tespit etmektir.

1 Eylül 2019 - 31 Ağustos 2024 dönemini kapsayan en son sistematik literatür taramasında, FemoSeal™ VCS hakkında klinik güvenilirlik ve performans verileri sağlayan 29 yayımlanmış çalışma belirlenmiştir. Yirmi üç referans, dokuz çalışmada FemoSeal™ VCS'nin etiket üzeri kullanımını ve etiket dışı kullanımını bildirmiştir. Genel olarak, FemoSeal™ VCS kullanımına özel çalışmaların literatür incelemesi, AB'de perkütan vasküler kateterizasyon prosedürleri uygulanan hastaları temsil eden bir çalışma popülasyonunu göstermektedir. Hakem denetiminden geçmiş olan bu 23 etiket üzeri yayının listesi için **Bölüm 3'e** bakın.

Klinik performans aşağıdaki ölçütlerle değerlendirilmiştir:

- Perkütan ortak femoral arter kapatma işlemi için hemostaz süresi, Son Teknoloji'den daha iyi veya ona benzerdir.

- Ortak femoral arterin perkütan olarak kapatılması için ambülasyon süresi, Son Teknoloji'den daha iyi veya ona benzerdir.
- Postoperatif komplikasyon oranı, mevcut bakım standartlarına benzer veya ondan daha düşüktür.

Bu klinik performans ölçümlerine dayanarak, bu literatür incelemesinde FemoSeal™ VCS'nin 7 Fr veya daha küçük bir prosedür kılıfı kullanılarak perkütan kateterizasyon uygulanan hastalarda femoral arter ponksiyonunun (arteriyotomi) kapatılmasında başarıyla kullanılabileceğini göstermiştir. Vakalardaki hastaların çoğunluğunda (%79,65-100) tam hemostaz sağlandı ve medyan hemostaz süresi 0,5 dakika ve ortalama taburcu olma süresi ise 3 gündü. Hastaların %69,2-86,7'si, ortalama 349 dakikalık ameliyat sonrası yatak istirahati ile kapatma işleminden 5 saat sonra ambüle edilebilmiştir. Vakaların %3,68-4'ünde FemoSeal™ VCS arızası gözlenmiştir ve prosedürlerin %0,9-4,4'ünde ek manuel kompresyon gerekli olmuştur.

Klinik güvenlik, aşağıdakiler dahil ancak bunlarla sınırlı olmamak üzere advers olaylarla değerlendirilmiştir:

- Kanama
- Hematom
- Psödoanevrizma
- Morluk
- Arteriyovenöz Fistül
- Enfeksiyon
- Ölüm

Dâhil edilen çalışmalarda bu advers olayların her biri için FemoSeal™ VCS'de bildirilen görülme oranı, manuel kompresyon ve diğer vasküler kapatma cihazları için geçmişte bildirilen orandan daha az veya buna benzer olmuştur.

10 vaka raporu gözden geçirilerek herhangi bir advers olay belirlenmemiştir çünkü yeni, beklenmeyen, ortaya çıkan veya kabul edilemez riskler tespit edilmemiştir.

Tanısal anjiyografi veya girişimsel operasyonları sırasında FemoSeal™ VCS kullanımının genel etkinliği; cinsiyet, yaş, hasta anatomisi, komorbiditeler gibi çeşitli faktörlere bağlıdır, ponksiyon bölgesinin anatomik yerleşimi, cerrahın deneyimi, VCD yerleştirme yöntemi ve ameliyat sonrası bakım gibi birden fazla etmene bağlıdır. Hemostazın sağlanması da dâhil elde edilen teknik başarıya ek olarak FemoSeal™ VCS, femoral arter ponksiyonundan sonra vasküler kapatmaya göre hemostaz süresinin kısılması ve ambülasyon süresinin kısılması gibi klinik faydalar sağlamıştır. FemoSeal™ VCS'nin performans sonuçları, amaçlanan şekilde kullanıldıklarında bu tür cihazlar için beklenenlerle tutarlıdır. Mevcut arama dönemi sırasında elde edilen referanslardan bazıları, çalışma konusu cihazın ortak femoral arter dışındaki anatomik bir konumda ve >7 Fr arteriyotomilerin kapatılması için kullanıldığını göstermiştir. Bu durum, etiket dışı olarak kabul edilir.

Gözden geçirme sırasında cihazın bilinmeyen yan etkileri, ortaya çıkan riskleri veya olası sistematik yanlış kullanımı tespit edilmemiştir. Ancak FemoSeal™ VCS eğitimli doktorlar tarafından dikkatli bir şekilde kullanılırsa tıbbi cihaz yararlı ve gerekli bir klinik cihaz olarak işlevini yerine getirecektir. Genel olarak hedef tedavi ve dolayısıyla FemoSeal™ VCS, vasküler erişimle ilgili komplikasyonların tedavisinde şu anda mevcut olan klinik ihtiyacı gidermektedir.

Genel olarak, bu literatür taramasındaki veriler, klinik ortamda daha önce bilinmeyen herhangi bir performans veya güvenlik sorununu veya beklenenden daha yüksek / kabul edilebilir oranlarda meydana gelen advers etkileri tanımlamamıştır. Bu nedenle bu literatür taramasından, FemoSeal™ VCS'nin perkütan kateterizasyonu takiben arteriyotomide hemostaz için kompresyon sağlamak amacıyla kullanıldığında beklendiği gibi performans göstermeye devam ettiği ve ciddi güvenlik olaylarıyla ilişkili olmadığı sonucuna varılabilir.

#### 1.4.5 Pazarlama Sonrası Gözetimden Elde Edilen Verilerin Özeti

Proaktif bir PMS sistemi mevcuttur ve tüm şikâyetler aylık olarak ve dâhilî üretim prosedürlerine uygun şekilde incelenir. Şikâyet verileri, 1 Eylül 2019 - 31 Ağustos 2024 tarihleri arasında analiz edilmiştir. Genel olarak, 28 Tıbbi Cihaz Vijilans (MDV) Raporu ve 476 müşteri şikâyet raporu üretici firmaya sunuldu. Sunulan 28 MDV raporundan 27'si advers olaylarla, bir tanesi ise cihaz arızasıyla ilgiliydi. Raporlama döneminde iki ölüm yaşandı ancak bildirilen ölümlerin hiçbirinin çalışma konusu cihazla ilgili olmadığına karar verildi. Üretici firmaya yapılan 476 şikâyet arasında en yaygın şikâyet nedenleri yerleştirme zorluklarıydı (146 olay, %0,0142 oluşma oranı). Çıkma olaylarının arıza türü, %0,0126 (130 olay) oranıyla en sık oluşan ikinci durumdur.

FemoSeal™ Vascular Closure System'in dünya çapında 1.030.136'dan fazla satışı ve Avrupa Ekonomik Alanı'nda 827.843 satışı gerçekleşmiştir. Küresel satışlara dayalı şikâyetlerin hesaplanan sıklığı %0,046'dır. Genel müşteri şikâyet oranı çok düşüktür. Kullanım Talimatlarında ve risk dokümantasyonunda yer almayan yeni riskler belirlenmemiştir.

İstenmeyen yan etkilerin görülme oranları **Tablo 1.2'de** gösterilmiştir. Şikâyet yoluyla hiçbir yeni, beklenmeyen, ortaya çıkan veya kabul edilemez risk belirlenmemiştir. Bilinen istenmeyen yan etkilerin sıklığında veya şiddetinde önemli bir artış görülmemiştir.

#### 1.4.6 Genel Klinik Performans ve Güvenlilik Özeti

FemoSeal™ VCS, 7F (2,33 mm) veya daha küçük bir prosedürel kılıf kullanılarak perkütan kateterizasyon yapılan hastalarda ortak femoral arter ponksiyonunun (arteriyotomi) kapatılmasında kullanılır. Bu klinik değerlendirme, FemoSeal™ VCS'nin kullanım amacı ile ilgili mevcut pazarlama öncesi ve sonrası klinik verilerin ve literatürün kapsamlı bir analizine dayanmaktadır.

1 Eylül 2019 ile 31 Ağustos 2024 arasındaki dönemi kapsayan kapsamlı bir yayımlanmış literatür incelemesi gerçekleştirilmiştir. Elde edilen kanıtlar, FemoSeal™ VCS ile ilgili 29 çalışmayı içermiştir. Klinik değerlendirmede sağlanan kanıtlar, çalışma konusu cihazın endike

olduğu şekilde kullanıldığında güvenli ve etkili olduğunu ve normal kullanım koşulları altında cihazla ilişkili olabilecek herhangi bir risk veya istenmeyen yan etkinin, hastaya sağlanan faydalarla karşılaştırıldığında kabul edilebilir risk teşkil ettiğini ortaya koymaktadır. Çalışma konusu cihazların performans sonuçları, amaçlanan şekilde kullanıldıklarında bu tür cihazlar için beklenenlerle tutarlıdır.

FemoSeal™ VCS kullanımı ile ilişkili potansiyel istenmeyen yan etkiler, kanama ve hematoma gibi arteriyotomi kapatmanın alternatif yollarıyla yaygın olarak bildirilen advers olayları içerir. Genel olarak, FemoSeal™ VCS kullanımıyla bildirilen advers olayların meydana gelme oranları, manuel kompresyon ve benzer vasküler kapatma cihazlarıyla bildirilen oranlara benzerdir. Özellikle, kanama ve hematoma açısından FemoSeal™ VCS için bildirilen oranlar, benzer vasküler kapatma cihazları için bildirilen oranlardan daha düşüktür. Hem yayımlanan literatürden hem de pazarlama sonrası gözetimden bildirilen advers olayların her biri önceden tanımlanmıştır (bk. **Bölüm 1.3**).

FemoSeal VCS'nin klinik güvenlik ve performansına ilişkin mevcut veriler, bu vasküler kapatma cihazının kullanımından elde edilen hastalara olan yararların, Kullanım Talimatları uyarınca kullanıldığında ortaya çıkacak olası risklerden daha ağır bastığını göstermektedir.

Yukarıdaki bölümlerde belirtildiği gibi FemoSeal™ VCS için sağlanan veriler; değerlendirilen cihazla ilgili veriler (örneğin cihaz kullanımı, güvenlik sonuçları, klinik performans ve klinik faydalar), tespit edilen eş değer cihazlar ve Son Teknoloji çalışmasında listelenen benzer cihazlarla ilgili veriler arasındaki tutarlılığı göstermektedir.

Güvenlilik verilerinin çapraz analizi sonucunda aşağıdakiler arasında herhangi bir boşluk tespit edilmemiştir:

- Son Teknoloji çalışmasında belirtilen veriler
- Değerlendirilen cihaza özel veriler
- Risk Yönetimi Dosyalarında belirtilen veriler
- Etiket ve/veya kullanım talimatlarında belirtilen veriler (örneğin, kullanıcıya iletilecek rezidüel riskler).

Yayımlanmış, hakem denetiminden geçmiş klinik literatürde, şirket sponsorluğundaki klinik çalışmalarda ve pazarlama sonrası verilerin incelemesinde tespit edilen düşük komplikasyon oranlarıyla ve piyasadan geri çekmenin olmamasıyla klinik güvenlik kanıtlanmıştır.

Performansla ilgili herhangi bir endişe tespit edilmemiştir ve taranan literatürde FemoSeal™ VCS'nin üretici firmanın kullanım amacı ile tutarlı şekilde kullanıldığı görülmüştür.

## 1.5 Olası Tanı veya Tedavi Alternatifleri

Manuel kompresyon, geleneksel olarak vasküler kateterizasyonlardan sonra arteriyotomi bölgesinde hemostaz sağlamak için kullanılır. Manuel kompresyon, hastanın uzun süre (prosedürden sonra 8 saate kadar) hareketsiz kalmasıyla ve önemli rahatsızlık ve uzun hastanede kalış süreleriyle ilişkilendirilmiştir. Yakın zamanda gerçekleştirilen bir sistematik inceleme, manuel kompresyonla hemostazın sağlanması için medyan sürenin 20,8 dakika olduğunu ortaya koymuştur.<sup>1</sup>

Manuel kompresyona alternatifler, arteriyotomi bölgesine mekanik kompresyon uygulayan harici hemostatik cihazları içerir. Bu cihazlar hemostaz süresini veya ambülasyon süresini kısaltmaz, ancak manuel sıkıştırmayı mekanik sıkıştırma ile değiştirerek personel gereksinimlerini azaltır. Mekanik kompresyon kullanımı ile ilişkili advers olay oranları, manuel kompresyon ile ilişkili oranlara benzerdir.

FemoSeal™ VCS gibi vasküler kapatma cihazları, arteriyotomiye kapatmak için tasarlanmıştır. Hemostaz süresini kısaltmayı ve daha erken ambülasyon sağlamayı hedeflemektedirler. Piyasada bulunan 13 cihazı içeren yakın zamanda gerçekleştirilen bir sistematik inceleme, vasküler kapatma cihazı ile hemostazın sağlanması için medyan sürenin 5,4 dakika olduğunu ortaya koymuştur. Cihazların çoğu 4 ile 10 dakika arasında olacak şekilde her bir vasküler kapatma cihazı için medyan hemostaz süresi 1 dakika (FemoSeal™ VCS) ile 14 dakika arasında değişmiştir.<sup>1</sup>

Arteriyotomi bölgesinin kapanması, manuel kompresyonlar, eksternal hemostatik cihazlar veya vasküler kapama cihazları ile ilişkili olarak sık bildirilen advers olaylar arasında hematoma, erişim bölgesinde kanama, psödoanevrizma, arteriyovenöz fistül ve enfeksiyon sayılabilir. Aynı sistematik incelemede (34 randomize kontrollü çalışma, 14.401 hasta), kanamanın vasküler kapatma cihazlarında biraz daha yüksek olma eğiliminde olması dışında, manuel kompresyon ile vasküler kapatma cihazlarının kullanımı arasında advers olay oranlarının benzer olduğu görülmüştür.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*

## 1.6 Önerilen Kullanıcı Profili ve Eğitimi

FemoSeal™ Vascular Closure System cihazının amaçlanan kullanıcıları, ortak femoral arter yoluyla endovasküler prosedürler için arteriyel erişim ve kapama gerçekleştirme konusunda eğitim almış ve Terumo Medical Corporation FemoSeal™ doktor eğitim programına katılmış doktorlardır.

### 1.7 İlgili Uyumlaştırılmış ve Ortak Standartlar

| Standart Referans | Geçerli Uyumluluk Yılı/Rev | Açıklama                                                                                                                                 |
|-------------------|----------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070         | 2014/AMD1:2018             | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070      | 2014/A1:2018               | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Kılavuzu      | 20 Mayıs 2021              | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052        | 2015                       | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213        | 2017                       | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503        | 2020                       | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182        | 2019                       | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |
| EN ISO 13485      | 2016/A11:2021              | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 13485         | 2016                       | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 14644-1       | 2015                       | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                  |
| EN ISO 14644-1    | 2015                       | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                  |



| Standart Referans     | Geçerli Uyumluluk Yılı/Rev | Açıklama                                                                                                                                                                 |
|-----------------------|----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14644-2           | 2015                       | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2        | 2015                       | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3           | 2019                       | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3        | 2019                       | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1           | 2003                       | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1        | 2003                       | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2           | 2003/TC1:2004              | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| EN ISO 14698-2        | 2003/TC 1:2004             | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| USP <788>             | Yok                        | PARTICULATE MATTER IN INJECTIONS                                                                                                                                         |
| AB Farmakopesi 2.9.19 | Yok                        | Particulate Contamination: Sub-Visible Particles                                                                                                                         |
| IEC 62366-1           | 2015                       | Medical devices — Part 1: Application of usability engineering to medical devices                                                                                        |
| EN 62366-1            | 2015                       | Medical devices — Part 1: Application of usability engineering to medical devices                                                                                        |



| Standart Referans | Geçerli Uyumluluk Yılı/Rev | Açıklama                                                                                                             |
|-------------------|----------------------------|----------------------------------------------------------------------------------------------------------------------|
| EN ISO 14971      | 2019/A11:2021              | Medical devices — Application of risk management to Medical devices                                                  |
| ISO 14971         | 2019                       | Medical devices — Application of risk management to Medical devices                                                  |
| ASTM F1980        | 2016                       | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1    | 2020                       | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1       | 2018                       | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2    | 2006                       | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2       | 2006                       | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3    | 2014                       | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3       | 2014                       | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4    | 2017                       | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| ISO 10993-4       | 2017                       | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |
| EN ISO 10993-5    | 2009                       | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| ISO 10993-5       | 2009                       | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                                   |
| EN ISO 10993-6    | 2016                       | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                        |

| Standart Referans | Geçerli Uyumluluk Yılı/Rev | Açıklama                                                                                                                                   |
|-------------------|----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-6       | 2016                       | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                                              |
| EN ISO 10993-10   | 2023                       | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| ISO 10993-10      | 2021                       | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                                             |
| EN ISO 10993-11   | 2018                       | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| ISO 10993-11      | 2017                       | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                                            |
| EN ISO 10993-12   | 2021                       | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| ISO 10993-12      | 2021                       | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                                             |
| EN ISO 10993-17   | 2009                       | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-17      | 2002                       | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances                             |
| ISO 10993-18      | 2020/A1:2022               | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |
| EN ISO 10993-18   | 2020/A1:2022               | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process |
| EN ISO 10993-23   | 2021                       | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |
| ISO 10993-23      | 2021                       | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                   |

| Standart Referans | Geçerli Uyumluluk Yılı/Rev | Açıklama                                                                                                                                                                     |
|-------------------|----------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ASTM F2382        | 2018                       | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756         | 2017                       | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>          | Yok                        | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>         | Yok                        | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72    | 2019                       | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135      | 2014/A1:2019               | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135         | 2014/A1:2018               | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| EN ISO 10993-7    | 2008/A1:2022               | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                                    |
| ISO 10993-7       | 2008/A1:2019               | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                                            |
| EN 556-1          | 2024                       | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices              |

| Standart Referans | Geçerli Uyumluluk Yılı/Rev | Açıklama                                                                                                                                 |
|-------------------|----------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 11737-1    | 2018/A1:2021               | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products    |
| ISO 11737-1       | 2018/A1:2021               | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products    |
| EN ISO 11138-1    | 2017                       | Sterilization of health care products - Biological indicators - Part 1: General requirements                                             |
| ISO 11138-1       | 2017                       | Sterilization of health care products - Biological indicators - Part 1: General requirements                                             |
| EN ISO 11138-2    | 2017                       | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| ISO 11138-2       | 2017                       | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes |
| EN ISO 15223-1    | 2016                       | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| ISO 15223-1       | 2016                       | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements   |
| EN 1041           | 2008/A1:2013               | Information supplied by the manufacturer of medical devices                                                                              |
| EN ISO 11607-1    | 2020/A1:2023               | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |
| ISO 11607-1       | 2019/A1:2023               | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems  |

| Standart Referans | Geçerli Uyumluluk Yılı/Rev | Açıklama                                                                                                                                                                   |
|-------------------|----------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| EN ISO 11607-2    | 2020/A1:2023               | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ISO 11607-2       | 2019/A1:2023               | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes                                         |
| ASTM D4169        | 2016                       | Standard Practice for Performance Testing of Shipping Containers and Systems                                                                                               |
| ASTM F1886/F1886M | 2016                       | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                                                        |
| ASTM F2825        | 2018                       | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                                                   |
| ASTM F2096        | 2011 (R 2019)              | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                                                               |
| ASTM F88/F88M     | 2015                       | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                                                       |
| MDCG 2021-24      | 2021                       | Guidance on classification of medical devices                                                                                                                              |
| MDCG 2020-3       | 2020                       | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD |
| MDCG 2020-8       | 2020                       | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                             |
| MDCG 2020-7       | 2020                       | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                          |
| MDCG 2020-6       | 2020                       | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                       |

| Standart Referans | Geçerli Uyumluluk Yılı/Rev | Açıklama                                                                                                                                                                                                                                                      |
|-------------------|----------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2019-9 v1    | 2022                       | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                                                                                                      |
| MDCG 2019-8 v2    | 2020                       | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices                                                                            |
| MDCG 2020-15      | 2020                       | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                                                                                                      |
| MDCG 2021-11      | 2021                       | Guidance on Implant Card – ‘Device types’                                                                                                                                                                                                                     |
| MDCG 2021-19      | 2021                       | Guidance note integration of the UDI within an organisation’s quality management system                                                                                                                                                                       |
| MDCG 2018-1 v4    | 2021                       | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                                                                                                |
| MDCG 2019-2       | 2019                       | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                                                                                            |
| MDCG 2019-1       | 2019                       | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                                                                                            |
| MDCG 2018-7       | 2018                       | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6       | 2018                       | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |
| MDCG 2018-4       | 2018                       | MDCG 2018-4 Annex: UDI database Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                                                                                                  |

| Standart Referans   | Geçerli Uyumluluk Yılı/Rev | Açıklama                                                                                                                                                                                      |
|---------------------|----------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2018-3 v1      | 2020                       | Guidance on UDI for systems and procedure packs                                                                                                                                               |
| MDCG 2021-25        | 2021                       | Regulation (EU) 2017/745 - application of MDR requirements to ‘legacy devices’ and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC |
| Meddev 2.12-2 Rev 2 | 2012                       | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                        |

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### 3.0 REVİZYON GEÇMİŞİ

| SSCP revizyon numarası    | Yayımlanma tarihi | Değişiklik açıklaması                                                   | Onaylanmış Kuruluş (NB) tarafından onaylanan revizyon                                                                                                                                                                                                                                                               |
|---------------------------|-------------------|-------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022              | 20 Ocak 2023      | İlk Baskı, MDR CE sertifikası üzerine                                   | <input checked="" type="checkbox"/> Evet<br>Doğrulama dili: English<br><input type="checkbox"/> Hayır (yalnızca SSCP'nin henüz NB tarafından onaylanmadığı IIa veya bazı IIb sınıfları implante edilebilir cihazlar (MDR, Madde 52 (4) 2. paragraf) için geçerlidir)<br><input type="checkbox"/> Diğer (açıklayın): |
| SSCP-FS-2023 - Revizyon 1 | 15 Mart 2024      | 1 Ocak 2019 ile 31 Aralık 2023 arasındaki dönem için güncellenmiştir.   | <input checked="" type="checkbox"/> Evet<br>Doğrulama dili: English<br><input type="checkbox"/> Hayır (yalnızca SSCP'nin henüz NB tarafından onaylanmadığı IIa veya bazı IIb sınıfları implante edilebilir cihazlar (MDR, Madde 52 (4) 2. paragraf) için geçerlidir)<br><input type="checkbox"/> Diğer (açıklayın): |
| SSCP-FS-2024 Revizyon 1   |                   | 1 Eylül 2019 ile 31 Ağustos 2024 arasındaki dönem için güncellenmiştir. | <input type="checkbox"/> Evet<br>Doğrulama dili: English<br><input type="checkbox"/> Hayır (yalnızca SSCP'nin henüz NB tarafından onaylanmadığı IIa veya bazı IIb sınıfları implante edilebilir cihazlar (MDR, Madde 52 (4) 2. paragraf) için geçerlidir)<br><input type="checkbox"/> Diğer (açıklayın):            |

|                            |               |                                                              |                                                                                                                                                                                                                                                                                                                                            |
|----------------------------|---------------|--------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2024<br>Revizyon 2 | June 20, 2025 | Doğrulama için NSAI<br>sorgularına göre revize<br>edilmiştir | <input checked="" type="checkbox"/> Evet<br>Doğrulama dili: English<br><br><input type="checkbox"/> Hayır (yalnızca SSCP'nin<br>henüz NB tarafından<br>onaylanmadığı IIa veya bazı IIb<br>sınıfları implante edilebilir<br>cihazlar (MDR, Madde 52 (4)<br>2. paragraf) için geçerlidir)<br><br><input type="checkbox"/> Diğer (açıklayın): |
|----------------------------|---------------|--------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

**Огляд безпеки та клінічних характеристик**  
**Система для закриття місця пункції судини FemoSeal™**

|                                                                                             |                                                                                              |
|---------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|
| <b>Виробник</b>                                                                             | Terumo Medical Corporation<br>265 Davidson Ave, Suite 320<br>Somerset, NJ 08873 USA          |
| <b>SRN виробника</b>                                                                        | US-MF-000019594                                                                              |
| <b>Представник керівництва/особа,<br/>відповідальна за дотримання<br/>нормативних вимог</b> | Кімберлі Фейтл (Kimberly Feitl)<br>Vice President, Quality                                   |
| <b>Основний UDI-DI</b>                                                                      | 38970FS79                                                                                    |
| <b>Номер EMDN</b>                                                                           | C900199 – Системи для гемостазу – Інше                                                       |
| <b>Клас виробу</b>                                                                          | III клас                                                                                     |
| <b>Рік отримання маркування CE</b>                                                          | 2005                                                                                         |
| <b>Представник в ЄС</b>                                                                     | Terumo Europe, N.V.<br>Interleuvenlaan 40, 3001<br>Leuven<br>Belgium<br>SRN: BE-AR-000001433 |
| <b>Уповноважений орган</b>                                                                  | NSAI<br>CE 0050                                                                              |

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Цей огляд безпеки та клінічних характеристик (SSCP) призначений для надання публічного доступу до оновлених даних щодо основних аспектів безпечності та клінічної ефективності системи для закриття місця пункції судини (vascular closure system, VCS) FemoSeal™.

Стислий огляд даних щодо безпечності та клінічної ефективності пристрою, призначений для користувачів/медичних працівників, наведений в **розділі 1.0**.



## **1.0 ІНФОРМАЦІЯ ДЛЯ КОРИСТУВАЧІВ / МЕДИЧНИХ ПРАЦІВНИКІВ**

SSCP не замінює інструкції із застосування, що є основним документом, призначеним для забезпечення безпечного використання пристрою, і не містить рекомендацій для користувачів або пацієнтів щодо діагностики чи лікування. SSCP не призначений для заміни обов'язкової інформації, що зазначається в картках з інформацією про пацієнта з імплантатом або в будь-яких інших обов'язкових документах.

### **1.1 Призначення пристрою**

#### **1.1.1 Показання до застосування**

Система для закриття місця пункції судини FemoSeal™ — це медичний пристрій, призначений для закриття місця проколу артерії після черезшкірної катетеризації через загальну стегнову артерію.

#### **1.1.2 Показання до застосування**

Система для закриття місця пункції судини FemoSeal™ використовується для закриття місця проколу загальної стегнової артерії (артеріотомії) у пацієнтів, які пройшли черезшкірну катетеризацію з використанням інтродьюсера 7F (2,33 мм) або меншого розміру.

#### **1.1.3 Протипоказання та/або обмеження**

Система для закриття місця пункції судини FemoSeal™ протипоказана до використання у пацієнтів з артеріотоміями, в яких застосовувалися інтродьюсери або пристрої розміром більше 7F (2,33 мм).

#### **1.1.4 Цільова популяція пацієнтів**

Безпечність та ефективність системи для закриття місця пункції судини FemoSeal™ оцінювалися у пацієнтів віком від 18 років, які пройшли черезшкірну катетеризацію з використанням інтродьюсера 7F (2,33 мм) або меншого розміру.

#### **1.1.5 Окремі категорії пацієнтів**

Безпечність та ефективність системи для закриття місця пункції судини FemoSeal™ не встановлені для таких категорій пацієнтів:

- Пацієнти з існуючим аутоімунним захворюванням.
- Пацієнти, яким проводиться процедура тромболізу.
- Пацієнти з клінічно вираженим захворюванням периферичних судин.

- Пацієнти з неконтрольованою артеріальною гіпертензією (систолічний тиск > 220 мм рт. ст. або діастолічний тиск > 110 мм рт. ст.).
- Пацієнти з порушенням згортання крові, включаючи тромбоцитопенію (кількість тромбоцитів < 100 000) або анемію (гемоглобін < 10 мг/дл).
- Пацієнти з внутрішнім просвітом загальної стегнової артерії діаметром менше 5 мм.
- Пацієнти з нирковою та/або печінковою недостатністю.
- Пацієнти з іншими релевантними супутніми захворюваннями.
- Пацієнти певного расового та/або етнічного походження.
- Пацієнти з інфарктом міокарда протягом останніх 72 годин.
- Пацієнти з судинним трансплантатом або стентом в місці проколу.
- Вагітні жінки та жінки, що годують груддю.
- Пацієнти віком до 18 років.

### 1.1.6 Призначені користувачі

Призначеними користувачами системи для закриття місця пункції судини FemoSeal™ є лікарі, які отримали належну підготовку з виконання артеріального доступу через загальну стегнову артерію та закриття місця пункції в рамках ендоваскулярних процедур і пройшли спеціальний інструктаж із застосування пристрою FemoSeal™ від компанії Terumo Medical Corporation.

## 1.2 Опис пристрою

### 1.2.1 Опис виробу

Система для закриття місця пункції судини FemoSeal™ виробництва Terumo Medical Corporation (TMC) — це виготовлений з матеріалу, що розсмоктується, пристрій для закриття судин, призначений для досягнення гемостазу стегнової артерії після черезшкірної катетеризації через загальну стегнову артерію.

Місце проколу судини закривається елементами системи FemoSeal™, які складаються з двох полімерних дисків, що розсмоктовуються, а саме з внутрішнього герметизувального елемента та зовнішнього блокувального диска, які утримуються разом за допомогою розсмоктуваного мультифіламентного шовного матеріалу. Таким чином, місце артеріотомії закривається механічно (див. **малюнок 1.1** і **малюнок 1.2**). Після розгортання

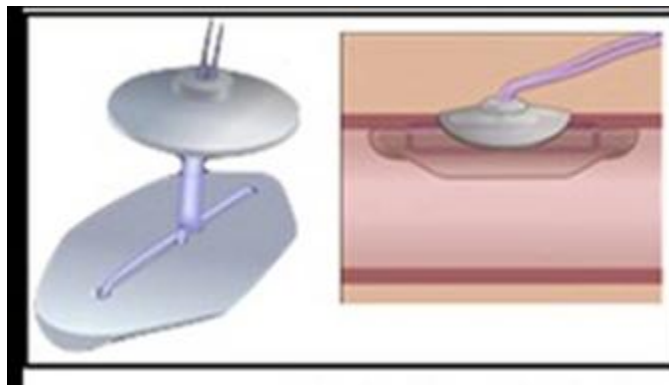
через конічну захисну канюлю зовнішній блокувальний диск просувається по шовному матеріалу і притискається до місця проколу, що призводить до механічного закриття місця проколу внутрішнім герметизувальним елементом і зовнішнім блокувальним диском. Внутрішній герметизувальний елемент та зовнішній блокувальний диск утримуються на місці завдяки мультифіламентному шовному матеріалу. Гемостаз досягається механічним шляхом. Запірні компоненти системи розкладаються шляхом гідролізу.

Запірні компоненти системи, що імплантуються — внутрішній герметизувальний елемент та зовнішній блокувальний диск — розкладаються через вісімнадцять (18) місяців, а мультифіламентний шовний матеріал розкладається шляхом гідролізу та поглинається навколишньою тканиною приблизно через два (2) або три (3) роки. Здатність запірних компонентів, що імплантуються, підтримувати компресію в місці артеріотомії перевірялася протягом восьми (8) годин. Продукти розпаду метаболізуються та виводяться із сечею або виділяються у вигляді вуглекислого газу через легені. В дослідженнях на тваринах ефектів накопичення не спостерігалось. Додатковими компонентами системи FemoSeal™, які контактують з живою тканиною або кров'ю під час процедури, є конічна захисна канюля, розширювач, трубка для тампонування, штовхач і провідник.

**Малюнок 1.1 Внутрішній герметизувальний елемент і зовнішній блокувальний диск, відповідно**

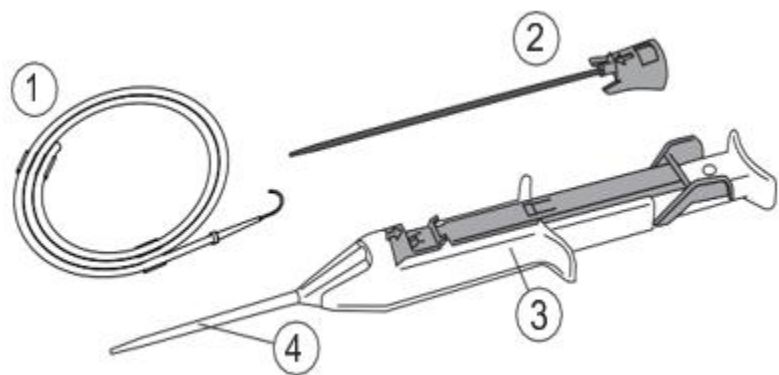


**Малюнок 1.2 Внутрішній герметизувальний елемент і зовнішній блокувальний диск в розгорнутому вигляді**



Пристрій FemoSeal™ поставляється в одній упаковці з розширювачем, провідником із зовнішнім діаметром 0,038 дюйма (0,97 мм) і довжиною 27,5 дюйма (70 см) і J-подібним випрямлячем, див **малюнок 1.3** нижче. Провідник міститься в поліетиленовій трубці. Усі частини пристрою вкладені у паперовий лоток, зафіксований всередині упаковки. В упаковці також міститься картка для зазначення інформації про пацієнта з імплантатом. Для належного функціонування система для закриття місця пункції судини FemoSeal™ не потребує додаткових допоміжних пристроїв, окрім розширювача та провідника, що поставляються в комплекті з виробом.

**Малюнок 1.3 FemoSeal™ VCS з провідником і розширювачем**



### 1.2.2 Матеріали та компоненти

В **таблиці 1.1** нижче перераховані компоненти системи FemoSeal™ VCS.

**Таблиця 1.1 Матеріали та компоненти системи FemoSeal™ VCS**

| Номер частини | Опис                                                     | Матеріали                                                                                                                                                                     |
|---------------|----------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1             | Провідник 0,038 дюйма (0,97 мм) з J-подібним випрямлячем | Провідник: неіржавна сталь 304<br>J-подібний випрямляч: поліпропілен, фіолетовий пігмент<br>Затискач: поліетилен<br>Трубка: поліетилен                                        |
| 2             | Розширювач FemoSeal                                      | Втулка: тетрагідрофуран, синій пігмент, полібутилентерефталат (ПБТ)<br><br>Трубка: поліетилен високої щільності (HDPE), чорний пігмент<br><br>Змазка: Силікон Dow Corning 360 |

|     |                      |                                                                                      |                                                                                                                                                                            |
|-----|----------------------|--------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 3/4 | Пристрій<br>FemoSeal | Формований RD7 — внутрішній герметизувальний елемент та зовнішній блокувальний диск* | Сополімер гліколіду, триметиленкарбонату, ε-капролактону і ТМП: триметилпропану (ініціатор)                                                                                |
|     |                      | Мультифіламентний шовний матеріал *                                                  | Сегментований сополімер L,L-лактиду, триметиленкарбонату, ε-капролактону і 1,3-пропандіолу (ініціатор)<br><br>Покриття є сополімером гліколіду, ε-капролактону та L-лізину |
|     |                      | Трубка для тампонування                                                              | Поліпропілен                                                                                                                                                               |
|     |                      | Штовхач                                                                              | неіржавна сталь 304V                                                                                                                                                       |
|     |                      | Повзунок                                                                             | Полібутилентерефталат (ПБТ)                                                                                                                                                |
|     |                      | Корпус                                                                               | Полібутилентерефталат (ПБТ)                                                                                                                                                |
|     |                      | Кнопка                                                                               | Полібутилентерефталат (ПБТ)                                                                                                                                                |
|     |                      | Кришка кнопки                                                                        | Поліоксиметилен (POM)/поліацетальний сополімер                                                                                                                             |
|     |                      | Муфта                                                                                | Полібутилентерефталат (ПБТ)                                                                                                                                                |
|     |                      | Розпірка                                                                             | Полібутилентерефталат (ПБТ)                                                                                                                                                |
|     |                      | Конус                                                                                | Поліпропілен                                                                                                                                                               |
|     |                      | Кришка корпусу                                                                       | Полібутилентерефталат (ПБТ)                                                                                                                                                |
|     |                      | Запобіжник                                                                           | Полібутилентерефталат (ПБТ), синій пігмент                                                                                                                                 |
|     |                      | Кришка муфти                                                                         | Полібутилентерефталат (ПБТ)                                                                                                                                                |
|     |                      | Прокладка трубки                                                                     | Силікон, твердість за Шором А 70                                                                                                                                           |
|     |                      | Прокладка корпусу                                                                    | Силікон, твердість за Шором А 50                                                                                                                                           |
|     |                      | Пружина                                                                              | неіржавна сталь 302                                                                                                                                                        |
|     |                      | Конічна захисна канюля                                                               | Поліпропілен<br>Силікон Dow Corning 360, гексан                                                                                                                            |

\* Частина пристрою, що імплантується; компоненти, що імплантуються, безпечні для МРТ

FemoSeal™ VCS є одноразовим медичним виробом, який стерилізовано гамма-опроміненням. Пристрій FemoSeal™ VCS сконструйований таким чином, що його не можна використовувати повторно.

## **Спосіб дії**

FemoSeal™ VCS забезпечує механічний гемостаз шляхом розміщення імплантованих запірних елементів всередині та ззовні загальної стегнової артерії. Механізм, що запобігає кровотечі, реалізується завдяки внутрішньому герметизувальному елементу, що закриває місце проколу, і зовнішньому блокувальному диску, який утримує внутрішній герметизувальний елемент в потрібному положенні.

### **1.2.3 Клінічна перевага**

Відносно закриття судини після пункції загальної стегнової артерії FemoSeal™ VCS має такі клінічні переваги:

- Скорочення часу до досягнення гемостазу<sup>1</sup>
- Скорочення часу до відновлення здатності пацієнта пересуватися<sup>1</sup>

1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). *Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international*, 27, 32–44.

### **1.2.4 Попередні покоління або варіанти пристрою**

- Перша версія пристрою FemoSeal™ VCS (№11200) продавалася на європейському ринку протягом 2005 і частково 2006 років.
- Поточна версія пристрою FemoSeal™ VCS (№11202) з покращеною системою доставки представлена на ринку з 28 березня 2006 року.

### **1.2.5 Приналежності, призначені для використання з виробом**

Пристрій FemoSeal™ поставляється в одній упаковці з розширювачем, провідником із зовнішнім діаметром 0,038 дюйма (0,97 мм) і довжиною 27,5 дюйма (70 см) і J-подібним випрямлячем. Провідник — це єдина приналежність, призначена для використання з пристроєм FemoSeal™. J-подібний випрямляч є компонентом провідника, а розширювач є компонентом пристрою FemoSeal™. Тому приналежністю вважається тільки провідник. Провідник міститься в поліетиленовій трубці. Усі частини пристрою вкладені у паперовий лоток, зафіксований всередині упаковки. В упаковці також міститься картка для зазначення інформації про пацієнта з імплантатом. Для належного функціонування система для закриття місця пункції судини FemoSeal™ не потребує додаткових допоміжних пристроїв, окрім розширювача та провідника, що поставляються в комплекті з виробом.

### **1.2.6 Інші пристрої та продукти, призначені для використання з цим виробом**

FemoSeal™ VCS не потребує додаткових пристроїв для належного функціонування.

### 1.3 Ризики та попередження

#### 1.3.1 Залишкові ризики та небажані ефекти

Відомі або передбачувані побічні явища, шкода здоров’ю та ускладнення, пов’язані з використанням системи FemoSeal™ VCS в результаті залишкових ризиків, перераховані в **таблиці 1.2**. Частоту розраховано на основі результатів аналізу даних про ризики та даних післямаркетингового нагляду з 1 вересня 2019 року по 31 серпня 2024 року. Застосування FemoSeal™ VCS не пов’язане з невідомими залишковими ризиками, а всі відомі ризики перераховані у відповідній інструкції із застосування та враховані в процесі управління ризиками.

**Таблиця 1.2. Побічні явища/ускладнення при застосуванні FemoSeal**

| Шкода здоров’ю           | Частота виникнення (%) | Пом’якшувальні фактори                                                                                                                                                         |
|--------------------------|------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Алергічна реакція        | 0,0000                 | Дії та плани, спрямовані на максимальне зниження ризиків, стосувалися дизайну пристрою, інструкцій з виробництва, маркування готового продукту та належної підготовки лікарів. |
| Аневризма                | 0,0000                 |                                                                                                                                                                                |
| Артеріовенозна фістула   | 0,0001                 |                                                                                                                                                                                |
| Втрата крові/кровотеча   | 0,0280                 |                                                                                                                                                                                |
| Смерть                   | 0,0002                 |                                                                                                                                                                                |
| Екхімози                 | 0,0000                 |                                                                                                                                                                                |
| Емболія                  | 0,0000                 |                                                                                                                                                                                |
| Реакція на стороннє тіло | 0,0000                 |                                                                                                                                                                                |
| Гематома                 | 0,0027                 |                                                                                                                                                                                |
| Крововилив               | 0,0001                 |                                                                                                                                                                                |
| Інфекція                 | 0,0002                 |                                                                                                                                                                                |
| Запальна реакція         | 0,0000                 |                                                                                                                                                                                |
| Оніміння                 | 0,0000                 |                                                                                                                                                                                |
| Біль                     | 0,0000                 |                                                                                                                                                                                |
| Дискомфорт пацієнта      | 0,0004                 |                                                                                                                                                                                |
| Затримка процедури       | 0,0065                 |                                                                                                                                                                                |
| Псевдоаневризма          | 0,0004                 |                                                                                                                                                                                |
| Заочеревинна кровотеча   | 0,0002                 |                                                                                                                                                                                |

| Шкода здоров'ю                         | Частота виникнення (%) | Пом'якшувальні фактори |
|----------------------------------------|------------------------|------------------------|
| Сепсис                                 | 0,0000                 |                        |
| Тромбоемболія                          | 0,0000                 |                        |
| Тромбоз                                | 0,0001                 |                        |
| Окклюзія судини/ішемія нижніх кінцівок | 0,0002                 |                        |
| Перфорація судини                      | 0,0000                 |                        |
| Розсічення/розрив тканини судини       | 0,0003                 |                        |

### 1.3.2 Попередження й заходи безпеки

#### Попередження

1. Не використовуйте, якщо упаковку пошкоджено або стерильну бар'єрну систему порушено.
2. Не використовуйте після закінчення терміну придатності: функціональні характеристики біорозкладних компонентів можуть змінитися.
3. Не використовуйте, якщо якісь елементи виглядають пошкодженими або мають дефекти.
4. Використання системи FemoSeal™ у випадку ймовірності бактеріального забруднення інтродьюсера або навколишніх тканин може призвести до інфікування.
5. В разі підозри на прокол задньої стінки артерії або за необхідності декількох проколів не слід обмежуватися тільки системою FemoSeal™ для досягнення артеріального гемостазу. Додатково застосовуйте ручну або механічну компресію.
6. Якщо місце пункції знаходиться в області біфуркації стегнової артерії або дистальніше області біфуркації, систему FemoSeal™ не слід використовувати через ризик неправильного розташування внутрішнього герметизувального елемента. Це явище може призвести до ускладнень у вигляді кровотечі та/або порушення нормального кровотоку.
7. В разі стійкої артеріальної кровотечі з місця розрізу не відрізайте мультифіламентний шовний матеріал, доки не буде досягнуто гемостазу. Якщо гемостазу не досягнуто, закріпіть мультифіламентний шовний матеріал стерильною



раневою пов'язкою та застосуйте додаткову компресію до досягнення гемостазу. В разі стійкої артеріальної кровотечі можуть виникнути значні ускладнення, які можуть призвести до травмування або смерті пацієнта.

8. Не використовуйте систему FemoSeal™, якщо місце пункції знаходиться проксимальніше пахової зв'язки, оскільки це може призвести до заочеревинної гематоми.
9. Пацієнти з високим ризиком кровотечі можуть страждати від підвищеної втрати крові, що вимагає переливання крові.
10. Від'єднання внутрішнього диска потенційно може спричинити тромбоз та/або емболію.

### **Заходи безпеки**

1. Процедуру розгортання системи FemoSeal™ мають виконувати лікарі, які пройшли належну підготовку з використання цього пристрою.
2. Перед розгортанням системи FemoSeal™ виконайте обмежену ангіографію стегнової артерії або пункцію стегнової артерії під ультразвуковим контролем.
3. В нижченаведених випадках процедуру слід припинити:
  - Діаметр просвіту загальної стегнової артерії < 5 мм.
  - Стеноз та/або значні атеросклеротичні відкладення поблизу місця пункції загальної стегнової артерії.
  - Пункція виконується в області біфуркації стегнової артерії або дистально від області біфуркації.
  - Аномальні гілки артерії або судинні аномалії поблизу місця пункції загальної стегнової артерії.
4. За наявності гематоми слід проявляти особливу ретельність, щоб правильно ввести конічну захисну канюлю в артерію.
5. Застосовуйте техніку пункції однієї стінки. Не проколуйте задню стінку артерії.
6. При використанні системи FemoSeal™ завжди дотримуйтесь стерильності.
7. Система FemoSeal™ призначена лише для одноразового використання. Її не можна використовувати повторно або будь-яким способом повторно стерилізувати. Пристрій FemoSeal™ сконструйований таким чином, що його не можна використовувати повторно.
8. Якщо під час розгортання внутрішнього герметизувального елемента відчувається неочікуваний опір, припиніть процедуру.

9. Для правильного розгортання внутрішнього герметизувального елемента перемістіть великий палець так, щоб кнопка могла вільно повертатися у вихідне положення.
10. Перш ніж розгорнути зовнішній блокувальний диск, переконайтеся, що кінчик конусної захисної канюлі пристрою FemoSeal™ знаходиться під поверхнею шкіри. Зовнішній блокувальний диск може випадково розгорнутись над рівнем шкіри у пацієнтів із короткою відстанню між стегною артерією та шкірою.
11. Для правильного розгортання може знадобитися спочатку виконати розріз шкіри.
12. Якщо внутрішній герметизувальний елемент знаходиться всередині артерії, і при цьому неможливо повністю відтиснути кнопку та розгорнути зовнішній блокувальний диск, може знадобитися хірургічне втручання для видалення запірних елементів системи FemoSeal™.
13. В разі необхідності повторної пункції тієї самої стегнової артерії протягом 18 місяців пункцію слід виконувати щонайменше на відстані одного сантиметра від центральної лінії місця доступу попередньої системи FemoSeal™.
14. Проінструкуйте пацієнта про необхідність дотримуватися вказівок лікаря щодо огляду місця закриття.
15. Проінструкуйте пацієнта про необхідність носити із собою протягом наступних 18 місяців картку з інформацією про пацієнта з імплантатом.

### **Заходи безпеки під час виписки**

Перш ніж розглянути можливість виписки, огляньте пацієнта на наявність таких клінічних станів:

1. Кровотеча та/або гематома в місці закриття.
2. Біль під час ходьби.
3. Ознаки інфекції в місці закриття.

### **1.3.3 Коригувальні дії з експлуатаційної безпеки**

Протягом періоду з 01 вересня 2019 року по 31 серпня 2024 року була проведена одна коригувальна дія з експлуатаційної безпеки, пов'язана з FemoSeal™ VCS.

У 2022 році компанія Terumo добровільно вилучила з використання системи FemoSeal™ VCS через скарги на збої в процесі застосування та у зв'язку з випробуванням системи FemoSeal виробництва Elkton при випуску партії з метою вимірювання зусиль під час тампонування та витягнення. Загалом з обігу в Південній Кореї було вилучено 950 пристроїв.

### 1.4 Клінічна оцінка та післямаркетингове клінічне спостереження

В таблиці 1.3 наведено перелік базових досліджень, проведених з метою отримання системою FemoSeal™ VCS дозволу на широке застосування, а також післямаркетингових досліджень та заходів в рамках післямаркетингового спостереження. Версія пристрою, що використовувалася у відповідному дослідженні, вказана в таблиці нижче. Перша версія FemoSeal™ VCS (№11200) була на ринку до 2006 року. Наступна версія (№C11202), випущена на ринок у 2006 році, представлена на ринку на сьогоднішній день.

Таблиця 1.3 Короткий огляд базових досліджень

| Домаркетингове дослідження функціональних характеристик на тваринах                                                                                                                                                                                                     | Версія пристрою                     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 11200                               |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France). | 11200                               |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).         | 11200                               |
| Перше клінічне дослідження за участю людей                                                                                                                                                                                                                              |                                     |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB.                                                            | 11200                               |
| Завершені післямаркетингові клінічні дослідження                                                                                                                                                                                                                        |                                     |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006)                                                                                                                                                                                                                              | C11202<br>(поточна версія пристрою) |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)                                                                                                                                                                                       | C11202<br>(поточна версія пристрою) |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009)                                                                                                                                                                                          | C11202<br>(поточна версія пристрою) |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (2022)                                                                                                                                                  | C11202<br>(поточна версія пристрою) |
| Заплановані / поточні післямаркетингові клінічні дослідження                                                                                                                                                                                                            |                                     |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Protocol: Addressing Gaps Identified in CER-FS-2023                                                                                                                                                              | C11202<br>(поточна версія пристрою) |

| Заходи в рамках післямаркетингового спостереження                                                                               |                                     |
|---------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2020)                                                       | C11202<br>(поточна версія пристрою) |
| 20210298 – Guidewire Clinical Survey Report (2020)                                                                              | C11202<br>(поточна версія пристрою) |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2024) | C11202<br>(поточна версія пристрою) |

**1.4.1 Огляд результатів домаркетингових випробувань (досліджень на тваринах та клінічних досліджень)**

В таблиці 1.4 нижче перераховані всі домаркетингові дослідження — як клінічні, так і доклінічні.

Таблиця 1.4 Домаркетингові дослідження

| Домаркетингове дослідження функціональних характеристик на тваринах                                                                                                                                                                                                     |                                                                                 |                                   |                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------|-----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Назва дослідження                                                                                                                                                                                                                                                       | Рік / ким проводилося                                                           | Тип дослідження                   | Цілі                                                                                                                                                                                                                                               | Етапи                                                                                                                                                                                                                                                                                                                                                                                                         | Потенційні критерії прийнятності                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vasculature System. Functional Implantation Test in Sheep 12-, 15-, and 18-month Time Periods. (R1051-1), 2000, Radi Medical System AB (performed by Biomatech, France). | 2000<br>Radi Medical Systems AB<br><br>Проводилося компанією Biomatech, Франція | Дослідження на тваринах; пошукове | Дослідження проводилося з метою оцінити біосумісність та біофункціональність біорозкладаного імплантату, призначеного для досягнення гемостазу в судинній системі. В звіті наведено дані резервних тварин з дослідження № 862 (документ № 1051-01) | N = 3 дорослі вівці, 1 тварина на контрольний момент часу<br><br>Подальше спостереження для гістологічного аналізу, макроскопічної оцінки та ультраструктурного аналізу <ul style="list-style-type: none"> <li>12 місяців</li> <li>15 місяців</li> <li>18 місяців</li> </ul> Контрольне ультразвукове дослідження з кольоровою доплерографією — через 30 днів у місцях доступу до сонної та стегнової артерій | Прокідність артерій <ul style="list-style-type: none"> <li>Оцінка кровотоку після розгортання пристрою — зниження кровотоку на 2/3, пов’язане з тимчасовим артеріальним вазоспазмом в результаті процедури, обидва випадки на лівій загальній сонній артерії</li> <li>Ультразвукове дослідження з кольоровою доплерографією (4 тижні) — 3/3 (100 %) без значного зниження кровотоку через 30 днів після імплантації</li> </ul> Макроскопічні дослідження <ul style="list-style-type: none"> <li>12 місяців — прохідність підтверджена макроскопічно як відсутність анатомічно видимої оклюзії;</li> </ul> |

|  |  |  |  |  | <div> <div> <div>відсутність макроскопічних уражень, що свідчать про місцеву непереносимість (крововиливів, некрозу або неоваскуляризації);</div> <div>відмічалася інкапсуляція внутрішнього диска</div> <div> <div>• 15 місяців — макроскопічне дослідження не виявило ознак запалення; залишків внутрішніх або зовнішніх дисків не виявлено;</div> <div>інкапсуляційна тканина, розташована в області зовнішнього диска, не змінилася з моменту оцінки через 12 місяців</div> <div>• 18 місяців — макроскопічне дослідження не виявило ознак місцевої непереносимості, видимий зовнішній диск (3/3 випадків), повний розпад внутрішнього диска; 1/3 (ліва загальна сонна артерія) — ослаблення стінки артерії в місці імплантації (може бути пов'язане з розгортанням пристрою)</div> </div> </div> <div>Висновки</div> <div> <div>• В результаті макроскопічного дослідження через 12, 15 і 18 місяців після імплантації ознак некрозу, розпаду тканини чи утворення тромбів не виявлено.</div> <div>• Процес розпаду внутрішнього та зовнішнього дисків прогресував з 12 по 18 місяць та завершився через 18 місяців, в результаті чого область імплантації покрилася тканиною білуватого кольору.</div> </div> </div> |
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|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                                                                                                |                                                                                    |                                          |                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                 | <ul style="list-style-type: none"> <li>Результати гістологічного дослідження через 18 місяців свідчили про відсутність полімерного матеріалу і про наявність ендолумінальної фіброзної тканини. Некротичних, дегенеративних або тромботичних уражень не виявлено.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep 12-, 24-, and 36-Week Time-Periods. (R1050-1), 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002 Radi Medical System AB</p> <p>Проводилося компанією Biomatech, Франція</p> | <p>Дослідження на тваринах; пошукове</p> | <p>Дослідження проводилося з метою оцінити біосумісність біорозкладаного імплантату, призначеного для досягнення гемостазу в судинній системі.</p> | <p>Подальше спостереження (після імплантації)</p> <ul style="list-style-type: none"> <li>12 тижнів</li> <li>24 тижні</li> <li>36 тижнів</li> </ul> <p>N = 12 овець, 3 тварини на контрольний момент часу, 3 резервні тварини, забиті через 12, 15 і 18 місяців</p> <p>Місця імплантації — права та ліва стегнові артерії, права та ліва загальні сонні артерії</p> <p>Ультразвукове дослідження з кольоровою доплерографією</p> | <p><u>Прокідність сонної та стегнової артерій через 4 тижні</u></p> <ul style="list-style-type: none"> <li>Значне зниження кровотоку 0/12 (0 %)</li> </ul> <p><u>Значне зниження кровотоку відсутнє</u></p> <ul style="list-style-type: none"> <li>Серйозне порушення кровотоку, пов'язане з встановленням пристрою 0/12 (0 %)</li> <li>Зменшення кровотоку в лівій загальній сонній артерії 2/12 (16,6 %) через тимчасовий артеріальний вазоспазм (пов'язаний з хірургічним втручанням, а не з застосуванням пристрою)</li> </ul> <p><u>Порушення кровотоку за результатами подальшого спостереження</u></p> <p>12 тижнів – 0/12 (0 %)</p> <p>24 тижні – 0/12 (0 %)</p> <p>36 тижнів – 0/12 (0 %)</p> <p>Вимірювання артеріального тиску (3 вівці — 36 тижнів)</p> <ul style="list-style-type: none"> <li>Значного зниження кровотоку не виявлено</li> </ul> <p>Результати макроскопічного дослідження для оцінки інтеграції та розпаду матеріалів (0–4 ступінь)</p> <p><u>Сонні артерії</u></p> <p><u>Внутрішня сторона</u></p> |

|  |  |  |  |  | <p>- інкапсуляція<br/>12 тижнів – 1,3<br/>24 тижні – 0,8<br/>36 тижнів – 0,7</p> <p>- розпад матеріалу<br/>12 тижнів – 2,2<br/>24 тижні – 2,3<br/>36 тижнів – 0,7</p> <p><i>Зовнішня сторона</i></p> <p>- інкапсуляція<br/>12 тижнів – 2,0<br/>24 тижні – 1,0<br/>36 тижнів – 0,8</p> <p>- розпад матеріалу<br/>12 тижнів – 2,0<br/>24 тижні – 2,7<br/>36 тижнів – 3,2</p> <p><i>Стегнові артерії</i></p> <p><i>Зовнішня сторона</i></p> <p>- інкапсуляція<br/>12 тижнів – 1,0<br/>24 тижні – 2,7<br/>36 тижнів – 1,0</p> <p>- розпад матеріалу<br/>12 тижнів – 2,0<br/>24 тижні – 2,4<br/>36 тижнів – 3,0</p> <p><i>Внутрішня сторона</i></p> <p>- інкапсуляція<br/>12 тижнів – 2,0<br/>24 тижні – 1,2<br/>36 тижнів – 1,0</p> <p>- розпад матеріалу<br/>12 тижнів – 1,0<br/>24 тижні – 2,2<br/>36 тижнів – 3,0</p> <p><u>Результати гістологічного дослідження для оцінки інтеграції, розпаду матеріалу та запалення (середнє значення відповідних показників, індекс 0–4) n=6</u></p> <p><i>Сонні артерії</i></p> <p>Зовнішній фіброз<br/>12 тижнів – 2,3</p> |
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|  |  |  |  |  | <p>24 тижні – 2,3<br/>36 тижнів – 1,8<br/>Внутрішня неоінтима<br/>12 тижнів – 3,0<br/>24 тижні – 2,7<br/>36 тижнів – 3,3<br/>Розпад матеріалу<br/>12 тижнів – 1,7<br/>24 тижні – 3,0<br/>36 тижнів – 3 +<br/>Показники запалення (макрофаги)<br/>12 тижнів – 3,0<br/>24 тижні – 1,7<br/>36 тижнів – 1,7<br/><u>Стегнові артерії</u><br/>Зовнішній фіброз<br/>12 тижнів – 1,3<br/>24 тижні – 1,5<br/>36 тижнів – 1,7<br/>Внутрішня неоінтима<br/>12 тижнів – 3,7<br/>24 тижні – 3,3<br/>36 тижнів – 3,8<br/>Розпад матеріалу<br/>12 тижнів – 2,0<br/>24 тижні – 3,0<br/>36 тижнів – 3 +<br/>Показники запалення (макрофаги)<br/>12 тижнів – 3,5<br/>24 тижні – 1,8<br/>36 тижнів – 1,8<br/><br/><u>Прохідність за результатами гістоморфологічного дослідження</u><br/>Сонні артерії<br/>12 тижнів 74,0 %<br/>24 тижні 81,9 %<br/>36 тижнів 89,43 %<br/>Стегнові артерії<br/>12 тижнів – 42,2 %<br/>24 тижні – 73,21 %<br/>36 тижнів – 78,71 %<br/><br/><u>Прохідність судин (середній %)</u><br/>Сонні артерії<br/>12 тижнів 94,6 %</p> |
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|                                                                                                                                                                                                                                                                        |                                                                                      |                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                | <p>24 тижні – 96,7 %<br/>36 тижнів – 94,7 %<br/>Стегнові артерії<br/>12 тижнів – 66,9 %<br/>24 тижні – 63,6 %<br/>36 тижнів – 75,1 %</p> <p>Висновки</p> <ul style="list-style-type: none"> <li>Значних ознак місцевої непереносимості через 12, 24 або 36 тижнів виявлено не було (відсутність видимих запальних, некротичних або дегенеративних уражень).</li> <li>Значних побічних тканинних реакцій на встановлення пристрою зареєстровано не було.</li> <li>Розпад матеріалів імплантату був майже завершений через 36 тижнів.</li> </ul> |
| <p>Biocompatibility and Biofunctionality of a Biodegradable Implant to Achieve Haemostasis in the Vascular System. Functional Implantation Test in the Sheep and in the Pig for 5 Weeks, (R1052-01) 2002, Radi Medical System AB (performed by Biomatech, France).</p> | <p>2002<br/>Radi Medical Systems AB<br/>Проводилося компанією Biomatech, Франція</p> | <p>Дослідження на тваринах</p> | <p>Дослідження проводилося з ціллю оцінити біосумісність та біофункціональність біорозкладаного імплантату, призначеного для досягнення гемостазу в судинній системі. Досліджуваний пристрій вводився в отвір проколу в артеріях для досягнення гемостазу. Один диск вводився в прокол артерії, а інший використовувався для закріплення внутрішнього диска із зовнішнього боку артерії. Обидва диски вводилися через канюлю інтродьюсера. Диски призначалися для запобігання кровотечі і подальшого загоєння стінки судини, після чого</p> | <p>Період імплантації / спостереження становив 5 тижнів для всіх тварин</p> <p>4 вівці, 1 свиня</p> <p>14 запірних елементів</p> <p>8 запірних елементів були імплантовані 2 вівцям</p> <p>2 запірних елементи були імплантовані 1 свині</p> <p>Під час імплантації двох запірних елементів в одну стегнову артерію відстань між ними становила &gt; 30 мм</p> | <p>Реєструвалися всі небажані явища (запалення, некроз, крововилив або будь-яке інше ураження) або будь-які випадки утворення тонкого шару псевдоінтими. Особлива увага приділялася початковому етапу інтеграції пристрою в тканину, з особливим акцентом на інкапсуляції внутрішнього диска.</p> <p>Результати макроскопічного дослідження вказували на відсутність значущих ознак місцевої непереносимості або утворення тромбів. Макроскопічне дослідження не виявило різниці між вівцею та свинією після імплантації</p>                   |

|  |  |  | <p>мали розкладатися та поглинатися тканинами. Дослідження проводилося для збору та аналізу даних після функціональної імплантації пристрою вівцям і свиням з метою оцінити здатність імплантату підтримувати фізіологічну функцію при використанні в кровоносній системі, а також вивчити реакцію організму господаря та реакцію пристрою (фізична цілісність, тканинна інкапсуляція на момент забиття) і оцінити розкладання матеріалу імплантату</p> |  | <p>запірних елементів у стегнових артеріях. Результати макроскопічного дослідження вказували на відсутність значущих ознак місцевої непереносимості або утворення тромбів. Макроскопічне дослідження не виявило різниці між вівцею та свинею після імплантації запірних елементів у стегнових артеріях.</p> <p>Гістопатологічний аналіз місця імплантації в овець не виявив місцевих побічних реакцій. Внутрішній та зовнішній диски мали ознаки розкладання і в деяких випадках були розбиті на дрібніші частини. Внутрішні диски були повністю інтегровані в неоінтимальну тканину. У свині гістопатологічний аналіз виявив трохи більше ознак запалення навколо внутрішнього та зовнішнього дисків. У тварин обох видів застосування мультифіламентного шовного матеріалу супроводжувалося більшою кількістю ознак запалення, ніж застосування матеріалу диска, що є нормальним для плетених ниток через їхню більшу площу поверхні.</p> <p>Прохідність судин вимірювали через</p> |
|--|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

|                                                                                                                                                                                                              |                              |                                                   |                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                           | 5 тижнів трьома різними методами:<br>гістоморфометричним, гістоморфометричним у поєднанні з вимірюванням діаметра судин з використанням штангенциркуля та за допомогою ультразвукового дослідження з кольоровою доплерографією. Середня прохідність судин у овець становила від 60 до 80 % залежно від методу (12 спостережень). У свині середня прохідність судин становила від 40 до 80 % (2 спостереження). |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|---------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Перше клінічне дослідження за участю людей</b>                                                                                                                                                            |                              |                                                   |                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                |
| Назва дослідження                                                                                                                                                                                            | Рік / ким проводилося        | Тип дослідження                                   | Цілі                                                                                                                                                                                                                                                                                                                 | Етапи                                                                                                                                                                                                                                                                                                                                                                                                                     | Потенційні критерії прийнятності                                                                                                                                                                                                                                                                                                                                                                               |
| Multi-Centre Clinical Trial of the FemoSeal Vascular Closure System for Sealing Femoral Arterial Punctures After Diagnostic/Interventional Cardiology Procedures (EU-SE-001); 2004, Radi Medical Systems AB. | 2004 Radi Medical Systems AB | Відкрите багатоцентрове дослідження в одній групі | Цілі дослідження полягали в оцінці безпечності, робочих характеристик та ефективності системи для закриття місця пункції судини FemoSeal (система FemoSeal) загалом і окремо запірних елементів у пацієнтів, які проходять діагностичні або інтервенційні кардіологічні процедури з доступом через стегнову артерію. | Дослідження з 2 частин<br><br>Всього n = 80<br>Частина 1 n = 20<br>Частина 2 n = 60<br>Показання до застосування:<br>Частина 1 — діагностична катетеризація серця з використанням стегнової артерії в якості місця доступу<br>Частина 2 — пацієнти, які проходять діагностичні та інтервенційні кардіологічні процедури з використанням стегнової артерії як місця доступу<br><br>Подальше спостереження протягом 30 днів | Результати гемостаз, досягнутий за допомогою системи FS без компресії<br>- Частина 1 20/20 (100 %)<br>- Частина 2 58/60 (97 %)<br>Медіанний час до гемостазу під час процедури (частина 2) — 1,0 хвилини (діапазон: негайно — 8 хвилин)<br><br><u>Час до відновлення здатності пересуватися (хв.)</u><br>Частина 1 — медіана: 33,0<br>середнє: 67,8<br>Частина 2 —                                             |

|  |  |  |  |  | <div>медіана: 45</div> <div>середнє: 87,5</div> <div>Частота серйозних судинних ускладнень — 30-денне подальше спостереження</div> <div>Частина 1</div> <div>- Відсутність судинних ускладнень 20/20 (100 %)</div> <div>Частина 2</div> <div>Псевдоаневризма 1/59 (1,69 %)</div> <div>Неефективність процедури</div> <div>Частина 1 – 0/20 (0 %)</div> <div>Частина 2 – 3/60 (5 %)</div> <div> <ul style="list-style-type: none"> <li>2 випадки внаслідок неможливості досягнення гемостазу без компресії</li> <li>1 випадок внаслідок серйозного судинного ускладнення, псевдоаневризми</li> </ul> </div> <div>Постійне виділення крові</div> <div>Частина 1 – 0/20 (0 %)</div> <div>Частина 2 – 8/60 (13 %)</div> <div>Гематома</div> <div>Частина 1 – 0/20 (0 %)</div> <div>Частина 2 – 6/60 (10 %)</div> |
|--|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

В рамках домаркетингового плану розробки FemoSeal™ VCS було проведено 3 функціональні тести на тваринах. У 2000 році, перед початком клінічних досліджень, було проведене дослідження на тваринах для оцінки біофункціональності FemoSeal™ VCS. В цьому дослідженні оцінювалася здатність запірних елементів підтримувати фізіологічну

функцію, а також розкладання цих елементів. Через 18 місяців матеріал внутрішнього та зовнішнього дисків став непомітним, його замінила ендолумінальна фіброзна тканина. За результатами цього дослідження була підтверджена здатність запірного елемента FemoSeal™ VCS підтримувати фізіологічну функцію під час використання в системі кровообігу.

В 2002 році було проведено дослідження на тваринах з метою оцінити біосумісність та біофункціональність біорозкладаного імплантату, FemoSeal™ VCS, призначеного для досягнення гемостазу в судинній системі. Загалом, розкладання матеріалу імплантату було майже завершено до 36 тижня, при цьому жодної значної побічної реакції з боку тканин не спостерігалось.

Під час іншого проведеного в 2002 році дослідження на тваринах оцінювали біосумісність та біофункціональність біорозкладаного імплантату, FemoSeal™ VCS, призначеного для досягнення гемостазу в судинній системі. Через 5 тижнів інкапсуляція дисків була завершена, мали місце ознаки розпаду матеріалу внутрішніх і зовнішніх дисків. За результатами цього дослідження була підтверджена здатність імплантату підтримувати фізіологічну функцію при використанні в системі кровообігу.

В рамках плану клінічного розвитку FemoSeal™ VCS компанія Radi Medical System AB провела домаркетингове клінічне дослідження. Результати цього дослідження не публікувалися і не викладалися в Інтернет. Дослідження приладу моделі №11200 проводилося в 2002–2004 рр. за європейським стандартом EN 540 (Клінічні дослідження медичних виробів для людей) і відповідно до Загальних принципів проведення клінічних випробувань ІСН та Керівництва з належної клінічної практики. Деталі цього дослідження викладені в звіті EU-SE-001. Результати дослідження описані у фінальному звіті компанії Radi Medical Systems AB «Багатоцентрове клінічне дослідження системи для закриття місця пункції судини FemoSeal для герметизації проколів стегнової артерії після діагностичних/інтервенційних кардіологічних процедур». Клінічне дослідження було проведено з використанням першої моделі FemoSeal™ №11200 і зосереджувалося на безпечності та ефективності запірних компонентів, що імплантуються. Єдиною відмінністю між першою моделлю №11200 і поточною моделлю C11202 є французький калібр, 6F і 7F відповідно, і вдосконалена система доставки. Клінічні переваги, показання до використання, принципи роботи та вихідні матеріали запірних елементів, що імплантуються (внутрішнього герметизувального елемента та зовнішнього блокувального диска), залишаються незмінними.

Пристрій призначався для пацієнтів, які проходили діагностичні або інтервенційні кардіологічні процедури з використанням стегнової артерії як точки доступу. Дослідження проводилося з метою оцінити безпечність, функціональні характеристики та ефективність

FemoSeal™ VCS. Дослідження проводилося як проспективне багатоцентрове відкрите дослідження в одній групі з 30-денним подальшим спостереженням.

Первинною кінцевою точкою ефективності був час до гемостазу, що визначався як відсутність швидкої кровотечі. Первинною кінцевою точкою безпечності була частота серйозних судинних ускладнень протягом 30 днів. Вторинні кінцеві точки включали час до відновлення здатності пересуватися, частоту невдалих процедур, частоту побічних явищ і робочі характеристики пристрою під час доставки та розгортання.

Пацієнти, включені в це дослідження, були дорослими, здатними дати інформовану згоду і придатними для вимірювання частоти пульсу принаймні на одній нозі. Пацієнти виключалися з дослідження за наявності будь-якого з наступних захворювань або станів:

- Захворювання периферичних судин в анамнезі
- Аутоімунне захворювання
- Встановлений розлад згортання крові — тяжка анемія
- МНС >1,5
- Інфаркт міокарда протягом останніх 72 годин
- Неконтрольована артеріальна гіпертензія, незважаючи на лікування
- Ожиріння, що унеможливило доступ за методикою Сельдингера
- Наявність судинного трансплантата або стента в місці артеріотомії
- Попередня іпсилатеральна пункція протягом останніх 3 місяців
- Тривалість життя < 6 місяців

Крім того, пацієнтів обстежували під час операції та виключали з дослідження, якщо спостерігалось будь-що з наступного:

- Діаметр просвіту загальної стегнової артерії < 5 мм
- Гілки артерії в межах 2 см проксимальніше місця пункції
- Виражений стеноз в межах 3 см від місця пункції
- Застосування інтродьюсера > 6 Fr в процесі попередньої процедури
- Пункція в області біфуркації стегнової артерії або дистально від області біфуркації
- Множинні пункції стегнової артерії
- Підтверджений або підозрюваний прокол задньої стінки стегнової артерії

- Велика гематома (2:6 см) після завершення процедури
- Труднощі при введенні інтродьюсера в процесі попередньої процедури через звивистість тканини або судини

Це дослідження проводилося за єдиним протоколом у дві частини: до участі в частині 1 було включено 20 пацієнтів, потім був виконаний аналіз безпечності, після чого ще 60 пацієнтів були включені в дослідження для участі в частині 2.

Середній вік пацієнтів, включених в частину 1, становив 65,9 років, 70,0 % пацієнтів були чоловіками, і 95 % пацієнтів приймали супутні ліки. Середній вік пацієнтів, включених в частину 2, становив 63,8 років, 78 % були чоловіками, і 100 % приймали супутні ліки.

Придатними до участі в дослідженні вважалися пацієнти, які проходили діагностичну (частина 1 і частина 2) або інтервенційну (частина 2) катетеризацію серця. Процедури, що виконувалися пацієнтам в рамках дослідження, відповідали стандартам медичної допомоги в кожній із зареєстрованих лікарень. Після процедури у цих пацієнтів застосовувалася система FemoSeal™ VCS. Дані про пацієнтів збирали на вихідному рівні, під час процедури та через 1 день і 30 днів після процедури. Результати цього дослідження узагальнені в **таблиці 1.5** і вказують на те, що система FemoSeal™ VCS є безпечною і ефективною для використання в цій групі пацієнтів.

**Таблиця 1.5 Клінічні показники, зареєстровані в домаркетинговому дослідженні**

|                                                                                                                      | Частина 1    | Частина 2                 |
|----------------------------------------------------------------------------------------------------------------------|--------------|---------------------------|
| Кількість пацієнтів                                                                                                  | 20           | 60                        |
| Середній час до гемостазу                                                                                            | 1,2 хвилини  | 1,6 хвилини <sup>a</sup>  |
| Середній час до відновлення здатності пересуватися                                                                   | 72,2 хвилини | 87,5 хвилини <sup>b</sup> |
| Частота серйозних судинних ускладнень <sup>c</sup>                                                                   | 0 (0 %)      | 1 (2 %)                   |
| Кількість пацієнтів із побічними явищами                                                                             | 5 (25 %)     | 19 (32 %)                 |
| Неефективність процедури (визначається як серйозні судинні ускладнення, необхідність ручної компресії або те й інше) | 0 (0 %)      | 3 (5 %)                   |
| Несправності пристрою                                                                                                | 0 (0 %)      | 6 (10 %)                  |

*<sup>a</sup>На основі загального розміру вибірки 58 пацієнтів, оскільки у 2 пацієнтів гемостазу під час процедури досягнуто не було через попередні інсультальні пункції. У цих пацієнтів гемостаз був досягнутий через 7 хвилин та 37 хвилин.*

*<sup>b</sup>На основі загального розміру вибірки 59 пацієнтів: 1 пацієнт не був включений, оскільки він був підключений до апарату ШВЛ через набряк легенів і не міг рухатися більше тижня.*

*<sup>c</sup>Визначається як судинне ускладнення, що потребує переливання крові або хірургічного лікування, або місцева інфекція, що потребує введення антибіотиків, госпіталізації або продовження госпіталізації чи хірургічної обробки місця встановлення пристрою*

Під час частини 1 цього дослідження серйозних судинних ускладнень не спостерігалось. В частині 2 цього дослідження було зареєстроване 1 серйозне судинне ускладнення: псевдоаневризма, про яку повідомлялося протягом 1 дня після процедури. Ця подія вимагала компресії під ультразвуковим контролем та ін'єкції тромбіну в псевдоаневризму і призвела до продовження госпіталізації пацієнта.

З 5 небажаних явищ, про які повідомлялося в частині 1 дослідження, було 1 можливо пов'язане з пристроєм: швидка кровотеча через 1 день після процедури, яка була класифікована як несерйозне явище. З 19 небажаних явищ, про які повідомлялося в частині 2 дослідження, спостерігалися 3 випадки гематоми, пов'язані з пристроєм і класифіковані як несерйозні явища, і 6 явищ, можливо пов'язаних із пристроєм, а саме 3 випадки постійного виділення крові, 2 гематоми та біль у 1 нозі після фізичних вправ; всі явища були класифіковані як несерйозні.

У 3 пацієнтів, які брали участь в частині 2 цього дослідження, процедура була визнана невдалою: у 2 випадках через нездатність досягти гемостазу без застосування компресії та в 1 випадку через серйозне судинне ускладнення (псевдоаневризму). У частині 1 дослідження невдалих процедур не було.

З шести випадків несправностей пристрою, зафіксованих в частині 2, три не заважали процедурі, один був пов'язаний з помилкою користувача, в одному випадку мало місце протікання інтродьюсера і в одному випадку — поломка ниткового з'єднання. Останні дві проблеми були усунуті після оновлення пристрою, реалізованого в моделі C11202.

Результати подальшого спостереження через 6 місяців після частини 2 домаркетингового клінічного дослідження не повідомлялися через недотримання пацієнтами вимог до участі в дослідженні. Результати домаркетингового клінічного дослідження (EU-SE-001) тривалістю 30 днів, що відповідає періоду подальшого спостереження згідно з даними в спеціалізованій медичній літературі, свідчать про те, що система FemoSeal™ VCS безпечна і ефективна.



#### 1.4.2 Огляд результатів післямаркетингових клінічних досліджень

Було проведено 4 післямаркетингові клінічні дослідження. Ці дослідження описані в таблиці 1.6 нижче. Результати цих клінічних досліджень не публікувалися і не викладалися в Інтернет.

**Таблиця 1.6 Завершені післямаркетингові клінічні дослідження**

| Завершені післямаркетингові клінічні дослідження                                            |                                                           |                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                        |
|---------------------------------------------------------------------------------------------|-----------------------------------------------------------|-------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Назва дослідження                                                                           | Рік / ким проводилося                                     | Тип дослідження                                                               | Цілі                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Етапи                                                                                                                                                                                                                                                                                                        | Потенційні критерії прийнятності                                                                                                                                                                                                                                                                                                                                                                       |
| PMS FemoSeal® VCS #11202 (R1756-01) (2006) User Acceptability of New Packaging (SIS) (2006) | 2006<br>RADI                                              | Післямаркетингове дослідження, ступінь прийняття нової упаковки користувачами | Післямаркетингове дослідження, проведене з використанням оновленої моделі системи FemoSeal Vascular® №11202, яка має модифіковану систему доставки порівняно з першою моделлю, №11200, з метою оцінки робочих характеристик.<br><br>Дослідження проводилося з метою отримати відгуки про нову редакцію інструкцій із застосування та навчальний проект для лікарів і медсестер, підтвердити дані, отримані в результаті аналізу ризиків, і посприяти покращенню якості виробу. | 100 пацієнтів<br>• 63 чоловіка / 37 жінок<br>• Середній вік жінок — 68 років, чоловіків — 65 років<br><br>2 шведські лікарні, 6 лікарів<br><br>112 пристроїв<br><br>Дані, внесені до індивідуальних реєстраційних форм пацієнтів (CRF)<br><br>Запланований час спостереження — 30 хвилин з моменту звернення | Результати<br><br>1. Ілюстрації/вказівки в інструкціях із застосування розцінюються як інформативні та достатні<br><br>2. Негайний гемостаз (91/100)                                                                                                                                                                                                                                                   |
| Confirmatory Assessment of FemoSeal™ Vascular Closure System in 7F-Sheath. (2008)           | Dr. Nicolas Moes<br>Innsbruck Medical University, Austria | Післямаркетингова підтверджувальна оцінка                                     | Мета цього дослідження полягала в оцінці безпечності та ефективності системи FemoSeal®, що використовується під час звичайної клінічної процедури у пацієнтів, яким виконується діагностична катетеризація серця або черешкірна кардіохірургічна операція із застосуванням інтродьюсера 7F.                                                                                                                                                                                    | 50 пацієнтів послідовно<br><br>Показання до застосування: діагностична або інвазивна катетеризація серця через загальну стегнову артерію                                                                                                                                                                     | Первинні кінцеві точки<br>• Первинна кінцева точка ефективності — ЧДГ (час до гемостазу) з виділенням крові або без нього, але без будь-якого додаткової компресії, ручної чи механічної.<br>• Кінцева точка безпечності — частота небажаних явищ — незначних та значних судинних ускладнень та всіх інших небажаних явищ, серйозних та несерйозних, протягом дослідження (тобто до виписки пацієнта). |

|                                                                                |            |                               |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
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|                                                                                |            |                               |                                                                                                                                                                                                                                                                                                                                                                                               | <table><tr><td>n</td><td>50</td></tr><tr><td>men</td><td>35 (70%)</td></tr><tr><td>women</td><td>15 (30%)</td></tr><tr><td>PCI cases</td><td>15</td></tr><tr><td>age (yrs)</td><td>62.6±11.1</td></tr><tr><td>body mass index (kg/m²)</td><td>25.4±6.7</td></tr><tr><td>systolic BP (mmHg)</td><td>131.2±20.9</td></tr><tr><td>diastolic BP (mmHg)</td><td>77.9±10.6</td></tr><tr><td>diabetes mellitus</td><td>9 (18%)</td></tr><tr><td>arterial hypertension</td><td>34 (68%)</td></tr><tr><td>previous coronary intervention</td><td>13 (26%)</td></tr><tr><td>preprocedure aspirin</td><td>50 (100%)</td></tr><tr><td>preprocedure clopidogrel</td><td>50 (100%)</td></tr><tr><td>Procedural unfractionated heparin</td><td>15 (30%)</td></tr><tr><td>Procedural abciximab</td><td>2 (4%)</td></tr></table> | n                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 50 | men | 35 (70%) | women | 15 (30%) | PCI cases | 15 | age (yrs) | 62.6±11.1 | body mass index (kg/m²) | 25.4±6.7 | systolic BP (mmHg) | 131.2±20.9 | diastolic BP (mmHg) | 77.9±10.6 | diabetes mellitus | 9 (18%) | arterial hypertension | 34 (68%) | previous coronary intervention | 13 (26%) | preprocedure aspirin | 50 (100%) | preprocedure clopidogrel | 50 (100%) | Procedural unfractionated heparin | 15 (30%) | Procedural abciximab | 2 (4%) | <p>Результати</p> <ul style="list-style-type: none"><li>• Середній час до гемостазу</li><li>• Діагностична процедура: 56,6 ± 29 секунд</li><li>• Втручання: 59,9 ± 16,2 секунди</li><li>• Всі пацієнти: 57,8 ±26,3</li><li>• Всі пацієнти могли без проблем пересуватися через 4 години постільного режиму.</li></ul> <p>Показники безпечності</p> <ul style="list-style-type: none"><li>• 49/50 (98 %) без судинних ускладнень до моменту виписки з лікарні</li><li>• Середній час до виписки: 2,6 доби</li><li>• В 1/50 (2 %) випадку незначна кровотеча наступного дня після виконаної ангиографії та досягнутої здатності безперешкодно пересуватися</li></ul> |
| n                                                                              | 50         |                               |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| men                                                                            | 35 (70%)   |                               |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| women                                                                          | 15 (30%)   |                               |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| PCI cases                                                                      | 15         |                               |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| age (yrs)                                                                      | 62.6±11.1  |                               |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| body mass index (kg/m²)                                                        | 25.4±6.7   |                               |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| systolic BP (mmHg)                                                             | 131.2±20.9 |                               |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| diastolic BP (mmHg)                                                            | 77.9±10.6  |                               |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| diabetes mellitus                                                              | 9 (18%)    |                               |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| arterial hypertension                                                          | 34 (68%)   |                               |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| previous coronary intervention                                                 | 13 (26%)   |                               |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| preprocedure aspirin                                                           | 50 (100%)  |                               |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| preprocedure clopidogrel                                                       | 50 (100%)  |                               |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Procedural unfractionated heparin                                              | 15 (30%)   |                               |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Procedural abciximab                                                           | 2 (4%)     |                               |                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Post-Marketing Surveillance (PMS) Study FemoSeal® VCS #11202 (R1756-03) (2009) | 2009 RADI  | Післямаркетингове дослідження | <p>Дослідження мало на меті збір інформації про те, чи стикалися клієнти/користувачі з будь-якими проблемами з новою упаковкою, особливо з нестерильною зовнішньою стороною пакета Tuvek/ПЕТ-ПЕ.</p> <p>Крім того, збиралася інформація про те, чи помічають лікарі будь-які відмінності в етапах застосування/розгортання пристрою порівняно з пристроями, які використовувалися раніше.</p> | <p>25 пристроїв</p> <p>4 шведські лікарні</p> <p>16/25 (64 %) пацієнтів проходили ЧКВ і застосовували потужні антикоагулянти</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | <p>Результати</p> <p>1. Проблеми, пов’язані з упаковкою — 21/25 (84 %) випадок застосування був успішним; 4/25 (16 %) були невдалими (1 випадок — тестування нового інтродьюсера, 1 випадок — на етапі відведення пристрою внутрішній диск пройшов крізь артеріотомію, кнопка піднялася, і зовнішній диск потрапив всередину розрізу, 2 випадки — негайного гемостазу не було досягнуто, незважаючи на відсутність проблем з розгортанням. )</p> <p>2. Негайний гемостаз: 19/25 (76 %) пацієнтів</p> |    |     |          |       |          |           |    |           |           |                         |          |                    |            |                     |           |                   |         |                       |          |                                |          |                      |           |                          |           |                                   |          |                      |        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |

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|                                                                                                                                 |                                 |                                                                           | Дослідження повинно було також виявити потреби в подальшому покращенні якості продукції.                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 3. Кровотеча 11/25 (44 %): у 9/25 (36 %) виділення крові/кровотеча, у 2/25 (8 %) гематоми<br>Загальна частота явищ: 19 %                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| The FemoSeal Vascular Closure System (VCS) Registry: A Prospective, Multi-Center, Observational Study in Europe (T138E4) (2022) | 2022/Terumo Medical Corporation | Проспективне, багатоцентрове, обсерваційне, післямаркетингове дослідження | Подальша демонстрація безпечності та ефективності FemoSeal™ VCS у досягненні гемостазу в місці доступу артерію у суб'єктів, яким виконують черезшкірні ендovasкулярні процедури. | <ul style="list-style-type: none"> <li>Подальше спостереження за пацієнтом через 30 днів (<math>\pm 7</math> днів) у формі відвідування лікарні або телефонного дзвінка.</li> <li>Включення в дослідження: грудень 2021 – липень 2022.</li> <li>230 включених в дослідження суб'єктів, яким показані діагностичні або інтервенційні ендovasкулярні процедури, під час яких використовується система FemoSeal™.</li> </ul> <p>3 дослідницькі центри в Європі: Франція (92 пацієнти), Німеччина (38 пацієнтів), Бельгія (100 пацієнтів).</p> | <ul style="list-style-type: none"> <li><b>Демографічні дані/супутні захворювання:</b> <ul style="list-style-type: none"> <li>- Стать: 161 чоловік (70 %)/69 жінок (30 %).</li> <li>- Середній вік: <math>70 \pm 12</math>.</li> <li>- ІМТ: <math>26,1 \pm 4,95</math> кг/м<sup>2</sup>.</li> <li>- Гіпертензія: 160 пацієнтів (69,6 %).</li> <li>- Дисліпідемія: 128 (55,7 %).</li> <li>- Ішемічна хвороба серця: 42 (18,3 %).</li> <li>- Курці на момент участі в дослідженні: 86 (37,6 %).</li> <li>- Курці в минулому: 66 (28,8 %).</li> <li>- Коронарна хвороба серця: 34 (14 %).</li> <li>- Інфаркт міокарда в анамнезі: 18 (7,8 %).</li> <li>- Реваскуляризація периферичних артерій: 12 (5,2 %) сонної артерії і 83 (37,5 %) артерії нижніх кінцівок.</li> <li>- Антитромбоцитарна терапія (на вихідному рівні): 211 (91,7 %), у тому числі 21 (9,1 %) подвійна антитромбоцитарна терапія (ПАТТ).</li> <li>- Пероральні антикоагулянти: 40 (17,4 %) пацієнтів.</li> </ul> </li> <li><b>Характеристики втручання:</b> <ul style="list-style-type: none"> <li>- Умови: стаціонарно 162 випадки (70,4 %), амбулаторно 68 випадків (29,6 %).</li> </ul> </li> </ul> |

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|  |  |  |  | <div> <div> <div>- Основне показання:<br/>переміжна кульгавість<br/>147 випадків (63,9 %).</div> <div>- Доступ: 35 випадків<br/>антеградний (15,3 %),<br/>194 випадки<br/>ретроградний (84,7 %).</div> </div> <div> <div>• Первинні кінцеві точки:</div> <div> <div>- Комбінована кінцева точка з оцінки безпечності (відсутність основних ускладнень з боку кінцівки, на якій проводилася процедура, протягом 6 годин після процедури) та ефективності (успішний гемостаз у місці пункції) була досягнута у 215/226 (95,1 %) [95% ДІ: 91,46; 97,55] пацієнтів з популяції для повного аналізу та 215/230 (93,5 %) [95% ДІ 89,47, 96,30] пацієнтів з популяції учасників дослідження, яким встановлено систему FemoSeal™.</div> <div>- Кінцева точка з оцінки ефективності була досягнута у 219/226 (96,9 %) ДІ [93,7, 98,7] пацієнтів.</div> <div>- Кінцева точка з оцінки безпечності була досягнута у 220/230 (95,2%) [95 % ДІ: 92,15, 97,90] пацієнтів.</div> </div> <div> <div>• Вторинні кінцеві точки:</div> <div> <div>- Відсутність незначних ускладнень у місці доступу протягом шести годин після процедури спостерігалася у 225/230 (97,8 %) [95% ДІ: 95,00; 99,29] пацієнтів.</div> </div> </div> </div> </div> |
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|  |  |  |  | <p>- Відсутність значних та незначних ускладнень у місці доступу протягом періоду часу від шести годин до 30 днів після процедури спостерігалася у 219/230 (95,2 %) [95% ДІ: 91,60; 97,59] пацієнтів.</p> <p>- Середній час досягнення гемостазу при застосуванні FemoSeal™ VCD: 0,42 (0,25; 0,50) хвилини.</p> <p>- Середній час до відновлення здатності пересуватися: 5,00 (4,54; 5,50) хвилин.</p> <p>- Середня тривалість перебування в лікарні: 23,98 (22,72, 25,00) годин.</p> <p>- Зручність використання FemoSeal™ VCS: «легко» або «дуже легко» розгортати в 98,7 % випадків («легко» розгортати у 21 (9,2 %), «дуже легко» розгортати у 205 (89,5 %) випадках) з відсутністю опору або низьким опором при розгортанні у 226 (98,3 %) випадках.</p> <p>У 152/230 (66,1 %) пацієнтів процедура виконувалася з використанням провідника, який входить до комплекту FemoSeal™ (зовнішній діаметр 0,038 дюйма) і рекомендований до використання разом з пристроєм FemoSeal™, без жодних повідомлень про недоліки пристрою чи побічні ефекти.</p> |
|--|--|--|--|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

Дослідження 2006 року проводилося з метою підтвердження безпечності та ефективності поточної версії пристрою з покращеною системою доставки та отримання відгуків про інструкції із застосування FemoSeal™ VCS і навчальну програму для медичних працівників. Дослідження включало 100 пацієнтів; первинна кінцева точка: досягнення гемостазу або необхідність у додатковій ручній чи механічній компресії. Це дослідження продемонструвало, що застосування FemoSeal™ VCS було успішним у більшості випадків (91 % досягли негайного гемостазу).

У дослідження 2008 року було включено 50 пацієнтів для оцінки безпечності та ефективності FemoSeal™ VCS при використанні під час звичайної клінічної процедури у пацієнтів, які проходили катетеризацію серця із застосуванням інтродьюсера 7 Fr. Основною кінцевою точкою дослідження був збір даних про час до гемостазу та час до відновлення здатності пересуватися, без додаткової компресії, ручної чи механічної. Результати дослідження свідчили про те, що середній час до гемостазу становив 57,8 секунди, і всі пацієнти могли рухатися після 4 годин постільного режиму.

Дослідження 2009 року мало на меті оцінити нову упаковку FemoSeal™ VCS. У дослідження було включено 25 пацієнтів. Основною кінцевою точкою була наявність у користувача проблем з упаковкою. Користувачі не відзначили жодних проблем щодо нової упаковки FemoSeal™ VCS. В процесі цього дослідження також збиралися дані про час до гемостазу.

Дослідження 2022 року мало на меті проактивний збір даних щодо безпечності та ефективності FemoSeal VCS у досягненні гемостазу в місці доступу через загальну стегнову артерію у суб'єктів, яким виконують черезшкірні ендovasкулярні процедури. У дослідження було включено 230 пацієнтів. Первинними кінцевими точками реєстрового дослідження є успішне виконання процедури (тобто успішний гемостаз у місці пункції) та зменшення серйозних ускладнень (таких як пошкодження судин, кровотеча в місці доступу, інфікування місця доступу, повторна ручна компресія та нові випадки гострої ішемії іпсилатеральної нижньої кінцівки, пов'язані з місцем доступу). Дослідження продемонструвало, що при використанні в реальних умовах FemoSeal™ VCS відповідає заявленим характеристикам і забезпечує ефективний гемостаз з низьким рівнем ускладнень у місці доступу у пацієнтів, яким виконують ендovasкулярні втручання на периферичних судинах. Про ефективність пристрою свідчить короткий час досягнення гемостазу та хороші відгуки користувачів про зручність використання. На підставі цього FemoSeal™ VCS може вважатися цінним пристроєм для закриття судини після пункції стегнової артерії.

### 1.4.3 Огляд результатів післямаркетингового клінічного спостереження

#### 1.4.3.1 Завершені заходи в рамках післямаркетингового спостереження

Короткий огляд завершених заходів в рамках післямаркетингового клінічного спостереження наведений в таблиці 1.7 нижче.

**Таблиця 1.7. Заходи в рамках післямаркетингового спостереження**

| Завершені заходи в рамках післямаркетингового клінічного спостереження    |                     |                                                                 |                                                                                                                                                                                                  |                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|---------------------------------------------------------------------------|---------------------|-----------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Назва заходу                                                              | Рік/ким проводилося | Тип дослідження                                                 | Цілі                                                                                                                                                                                             | Етапи                                                                                                                                                                  | Потенційні критерії прийнятності                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| 20210292 - FemoSeal Vascular Closure System Clinical Survey Report (2021) | 2021 TMC            | Післямаркетингове клінічне опитування — високоякісне опитування | Метою післямаркетингового опитування є проспективне документування відгуків щодо використання пристрою для закриття місця пункції судини FemoSeal™, представленого на ринку Європейського Союзу. | <ul style="list-style-type: none"> <li>120 випадків</li> <li>8 лікарів із стажем роботи понад 5 років</li> <li>Кілька країн у Європі</li> </ul>                        | <b>Оцінка пристрою за шкалою від 1 до 5 — оцінювані аспекти</b> <ul style="list-style-type: none"> <li>Критерії прийнятності <ul style="list-style-type: none"> <li>Бали від 3 до 5 вважаються позитивною оцінкою</li> <li>Усі аспекти повинні мати <math>\geq 80\%</math> позитивних оцінок</li> </ul> </li> <li>Результати <ul style="list-style-type: none"> <li>Жоден з оцінюваних аспектів не отримав <math>&gt; 20\%</math> негативних оцінок</li> <li>Скарг на виріб не було</li> </ul> </li> </ul> |
| 20210298 – 0.035” and 0038” Guidewire Clinical Survey Report (2021)       | 2021 TMC            | Післямаркетингове клінічне опитування — високоякісне опитування | Метою післямаркетингового опитування є проспективне документування відгуків щодо використання провідника                                                                                         | <ul style="list-style-type: none"> <li>Опитування щодо використання провідника 0,035 дюйма <ul style="list-style-type: none"> <li>106 опитувань</li> </ul> </li> </ul> | <b>Оцінка пристрою за шкалою від 1 до 5 — оцінювані аспекти</b> <ul style="list-style-type: none"> <li>Критерії прийнятності <ul style="list-style-type: none"> <li>Бали від 3 до 5 вважаються</li> </ul> </li> </ul>                                                                                                                                                                                                                                                                                      |

| Завершені заходи в рамках післямаркетингового клінічного спостереження                                                          |                  |                                                                 |                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                            |
|---------------------------------------------------------------------------------------------------------------------------------|------------------|-----------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                 |                  |                                                                 | діаметром 0,035 дюйма, що входить до комплекту пристрою для закриття місця пункції судини 6Fr Angio-Seal™ VIP Vascular Closure Device (VCD), та провідника діаметром 0,038 дюйма, що входить до комплекту пристрою для закриття місця пункції судини 8Fr Angio-Seal™ VIP VCD та системи для закриття місця пункції судини FemoSeal, представлених на ринку Європейського Союзу. | <ul style="list-style-type: none"> <li>○ 64 лікаря</li> <li>• Опитування щодо використання провідника 0,038 дюйма <ul style="list-style-type: none"> <li>○ 109 опитувань</li> <li>○ 55 лікарів</li> </ul> </li> <li>• 12 ретроспективних опитувань</li> </ul>                                                    | <ul style="list-style-type: none"> <li>○ позитивною оцінкою</li> <li>○ Усі аспекти повинні мати <math>\geq 80\%</math> позитивних оцінок</li> <li>• Результати <ul style="list-style-type: none"> <li>○ Усі провідники отримали прийнятні оцінки</li> <li>○ Скарг на виріб не було</li> </ul> </li> </ul>                                                                  |
| FemoSeal™ Vascular Closure System PMCF Clinical Survey Report: Addressing Gaps Identified in CER-FS-2021 and CER-FS-2022 (2023) | 2023–2024 TMC/TE | Післямаркетингове клінічне опитування — високоякісне опитування | Проспективне документування відгуків щодо використання FemoSeal VCS з провідниками, представленими на ринку Європейського Союзу.                                                                                                                                                                                                                                                | <ul style="list-style-type: none"> <li>• 126 опитувань</li> <li>• 7 центрів</li> <li>• 5 країн</li> <li>• 14 листопада 2023 р. – 11 червня 2024 р.</li> <li>• Медична спеціалізація лікаря: <ul style="list-style-type: none"> <li>○ Судинна хірургія</li> <li>○ Інтервенційна радіологія</li> </ul> </li> </ul> | <b>Оцінка пристрою за шкалою до 5 — оцінювані аспекти</b> <ul style="list-style-type: none"> <li>• Критерії прийнятності <ul style="list-style-type: none"> <li>○ Бали від 3 до 5 вважаються позитивною оцінкою</li> <li>○ Усі аспекти повинні мати <math>\geq 80\%</math> позитивних оцінок</li> <li>○ Якщо в цьому опитуванні згадуються небажані</li> </ul> </li> </ul> |



| Завершені заходи в рамках післямаркетингового клінічного спостереження |  |  |  |                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|------------------------------------------------------------------------|--|--|--|--------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                        |  |  |  | <div> <div>○ Ангіологія</div> </div> | <div> <div>явища, це мають бути явища, передбачені процесом управління ризиками.</div> <div> <div>• Демографічні дані пацієнтів</div> <div> <div>○ Жінки: 29,4 % (37/126)</div> <div>○ Чоловіки: 69,8 % (88/126)</div> <div>○ Без зазначення статі: 0,8 % (1/126)</div> <div>○ Вік &gt; 75 років: 31,7 %</div> </div> </div> <div> <div>• Результати</div> <div> <div>○ Провідник, що постачається з FemoSeal™ VCS: 101/126 (80,2 %).</div> <div>○ Тривалість процедури (хвилини): 63,4 (36,6) (середнє (стандартне відхилення)) ; 57,0 (36,0–81,0) (медіана (міжквартильний розмах))</div> <div>○ Усі оцінки ефективності</div> </div> </div> </div> |

| Завершені заходи в рамках післямаркетингового клінічного спостереження |  |  |  |  |                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|------------------------------------------------------------------------|--|--|--|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                        |  |  |  |  | <div> <div>FemoSeal™ VCS були сприятливи ми.</div> <div> <div>○ Усі оцінки провідника, що постачаєтьс я разом з FemoSeal™ VCS, були сприятливи ми.</div> <div>○ Одне (0,8 %) небажане явище: диски FemoSeal™ VCS були неправильно вирівняні, ймовірно, через використанн я жорсткого провідника (Boston Scientific Amplatz Super Stiff, 75 см, 0,035 дюйма), що вимагало ручної компресії для досягнення гемостазу.</div> </div> </div> |

Компанія Terumo Medical Corporation провела три високоякісні опитування користувачів-лікарів протягом поточного звітного періоду (01 вересня 2019 р. – 31 серпня 2024 р.).

Опитування щодо клінічного застосування системи FemoSeal™ допомогли зібрати проактивні клінічні дані щодо безпечності та ефективності FemoSeal™ VCS під час застосування в клінічній практиці. Опитування включало запитання, що стосувалися як самого пристрою, так і приналежностей, призначених для використання з пристроєм,

включно з провідником 0,038 дюйма, та їхньої прямої взаємодії. Опитування щодо клінічного застосування провідника дозволило отримати проактивні клінічні дані щодо безпечності та ефективності клінічного використання 0,038-дюймового провідника, що постачається з разом з FemoSeal™ VCS. Запитання цього опитування були зосереджені саме на загальних аспектах використання провідника, починаючи з введення через інтродьюсер в судинну систему і закінчуючи видаленням дроту.

FemoSeal™ VCS і 0,038-дюймовий провідник, що входить до складу пристрою, отримали прийнятні оцінки; після розгляду коментарів, зібраних завдяки високоякісним клінічним опитуванням, було подано шість (6) скарг щодо пристрою і дев'ять (9) повідомлень щодо провідника. Скарги розглядалися в контексті застосування пристрою FemoSeal і провідника і оцінювалися в рамках післямаркетингового нагляду компанії Terumo. Нових ризиків та/або рівнів ризику виявлено не було.

Одне опитування користувачів-лікарів було проведене у 2024 році в рамках заходів з післямаркетингового клінічного спостереження. Результати опитування показали, що оцінка ефективності та безпечності FemoSeal™ VCS загалом є дуже сприятливою. Також було продемонстровано сумісність інших провідників, окрім стандартних, що постачаються з FemoSeal™ VCS.

#### **1.4.3.2 Поточні/заплановані післямаркетингові клінічні спостереження**

Компанія ТМС має один поточний/запланований захід в рамках післямаркетингового клінічного спостереження. Буде проведене клінічне опитування для проспективного збору відгуків про використання представлених на ринку ЄС провідників з FemoSeal VCS. Опитування буде проводитися серед лікарів і матиме на меті з'ясувати, які провідники вони використовували під час процедури. Мета цього опитування — усунути недостатність даних, що виникла в результаті недостатньої кількості літератури та коментарів зовнішніх рецензентів щодо сумісності FemoSeal™ VCS з провідниками інших брендів, що не належать компанії Terumo. Відгуки включають дані про технічні аспекти, клінічну ефективність і безпечність при використанні пристрою з різними провідниками.

#### **1.4.4 Дані, отримані в результаті систематичного огляду літератури**

Компанія Terumo Medical Corporation проводить систематичні огляди літератури, щоб зібрати та оцінити дані про клінічну безпечність та ефективність на підставі опублікованих відомостей про результати досліджень пристрою FemoSeal™ VCS та/або подібних пристроїв. Метою щорічної перевірки опублікованої літератури є виявлення раніше невідомих побічних ефектів, моніторинг відомих побічних ефектів, виявлення нових ризиків і випадків можливого систематичного неправильного використання або використання не за призначенням пристрою FemoSeal™ VCS.

В ході останнього систематичного огляду літератури, який охоплював період з 1 вересня 2019 року по 31 серпня 2024 року, виявлено 29 опублікованих досліджень, що містили дані про клінічну безпечність та ефективність пристрою FemoSeal™ VCS. Двадцять три джерела згадували про використання FemoSeal™ VCS згідно з інструкцією та з відхиленнями від інструкції в рамках дев'яти досліджень. Згідно з джерелами інформації про дослідження, пов'язані з використанням FemoSeal™ VCS, досліджувана популяція складається з пацієнтів з ЕС, які проходять процедуру черезшкірної катетеризації судин. Перелік цих 23 рецензованих публікацій про застосування пристрою згідно з ухваленими показаннями див. в **розділі 3**.

Клінічну ефективність оцінювали за такими параметрами:

- Час до гемостазу коротший або аналогічний тому, що спостерігається при застосуванні подібних пристроїв для стандартної процедури черезшкірного закриття стегнової артерії.
- Час до відновлення здатності пересуватися коротший або аналогічний тому, що спостерігається при застосуванні подібних пристроїв для стандартної процедури черезшкірного закриття стегнової артерії.
- Частота післяопераційних ускладнень нижча або аналогічна тій, що спостерігається при застосуванні подібних пристроїв.

Виходячи з цих показників клінічної ефективності, дані з оглянутої літератури вказують на те, що FemoSeal™ VCS можна успішно використовувати для закриття пункції стегнової артерії (артеріотомії) у пацієнтів, які пройшли черезшкірну катетеризацію з використанням інтродьюсера 7 Fr або менше. Повний гемостаз був досягнутий у більшості пацієнтів (79,65–100 %), причому середній час до гемостазу становив 0,5 хвилин, а середній час до виписки — 3 дні. Від 69,2 до 86,7 % пацієнтів змогли пересуватися через 5 годин після закриття місця пункції судини, а середній час перебування в ліжку після процедури становив 349 хвилин. Неефективність FemoSeal™ VCS спостерігалася у 3,68–4 % випадків, а додаткова ручна компресія вимагалася під час виконання 0,9–4,4 % процедур.

Клінічну безпечність оцінювали на підставі частоти небажаних явищ, включаючи, серед іншого, наступні:

- Кровотеча
- Гематома
- Псевдоаневризма
- Синець
- Артеріовенозна фістула

- Інфекція
- Смерть

Частота виникнення кожного з цих небажаних явищ при застосуванні FemoSeal™ VCS в ході перерахованих досліджень була меншою або порівнянною з показниками частоти виникнення при застосуванні ручної компресії або інших пристроїв для закриття місця пункції судини.

За результатами перегляду 10 звітів про клінічні випадки небажаних явищ виявлено не було, оскільки не було виявлено нових, непередбачуваних або неприйнятних ризиків.

Загальна ефективність використання FemoSeal™ VCS під час діагностичної ангіографії або інтервенційних операцій залежить від багатьох факторів, таких як стать, вік, анатомічні особливості пацієнта, супутні захворювання, анатомічне розташування місця пункції, досвід хірурга, метод розгортання VCD, післяопераційний догляд тощо. Окрім технічного успіху, включно з досягненням гемостазу, FemoSeal™ VCS мала такі клінічні переваги в плані закриття судин після пункції стегнової артерії як скорочення часу до гемостазу та часу до відновлення здатності пересуватися. Результати застосування FemoSeal™ VCS відповідають очікуваням для цього типу пристроїв за умови використання за призначенням. У деяких джерелах, знайдених протягом поточного періоду пошуку, містилися дані про використання досліджуваного пристрою в анатомічному місці, відмінному від загальної стегнової артерії, та для закриття артеріотомій > 7 Fr, що вважається використанням не за призначенням.

Однак, якщо FemoSeal™ VCS використовується з обережністю кваліфікованими лікарями, вона функціонує як корисний та необхідний клінічний пристрій. Під час вивчення цих джерел не було виявлено жодних даних про невідомі побічні ефекти, нові ризики або можливе систематичне неправильне використання пристрою. Загалом, таргетна терапія, а отже, і система FemoSeal™ VCS, задовольняють клінічну потребу, яка існує на даний момент у лікуванні ускладнень, пов'язаних із судинним доступом.

Загалом, після вивчення даних, зазначених в цих джерелах інформації, не було виявлено жодних невідомих раніше проблем з ефективністю чи безпечністю застосування пристрою в клінічних умовах і жодних небажаних явищ, які виникали з вищою, ніж очікувалося/прийнятною частотою. Таким чином, з цього огляду літератури можна зробити висновок, що система FemoSeal™ VCS при використанні для забезпечення компресії з метою досягнення гемостазу при артеріотомії після черезшкірної катетеризації має очікувані функціональні характеристики і не пов'язана з серйозними подіями, які вказують на проблеми з безпечністю.

#### 1.4.5 Огляд результатів післямаркетингового нагляду

Виробник розробив проактивну систему післямаркетингових досліджень, а розгляд усіх скарг здійснюється щомісяця відповідно до внутрішніх виробничих процедур. Отримані скарги проаналізовані за період з 1 вересня 2019 року по 31 серпня 2024 року. Загалом виробнику було надіслано 28 звітів про результати контролю над виробами медичного призначення і 476 звітів про скарги користувачів. З 28 звітів про результати контролю над виробами медичного призначення 27 стосувалися небажаних явищ і один — несправності пристрою. Протягом звітного періоду сталося два смертельні випадки, але жодна з зареєстрованих смертей не була визнана пов'язаною з досліджуваним пристроєм. Серед 476 скарг, поданих виробнику, найпоширенішими причинами скарг були труднощі при розгортанні (146 випадків, частота виникнення 0,0142 %). Режим відмови під час витягнення пристрою є другою за частотою скаргою з частотою виникнення 0,0126 % (130 подій).

Система для закриття місця пункції судини FemoSeal™ була продана в кількості понад 1 030 136 штук по всьому світу та 827 843 штуки в Європейській економічній зоні. Обчислена частота скарг на основі глобальних продажів становить 0,046 %. Загалом, кількість скарг від користувачів дуже низька. Не було виявлено жодних нових ризиків, не вказаних в інструкціях із застосування та документації з інформацією щодо ризиків.

Показники частоти виникнення небажаних побічних ефектів наведені в **таблиці 1.2**. За результатами розгляду скарг не було виявлено нових непередбачуваних, нових або неприйнятних ризиків. Значного підвищення частоти або збільшення тяжкості відомих небажаних побічних ефектів не спостерігалось.

#### 1.4.6 Загальний огляд безпеки та клінічних характеристик

Система FemoSeal™ VCS використовується для закриття місця проколу загальної стегнової артерії (артеріотомії) у пацієнтів, які пройшли черезшкірну катетеризацію з використанням інтродьюсера 7F (2,33 мм) або меншого розміру. Ця клінічна оцінка базується на всебічному аналізі наявних клінічних даних за період домаркетингового і післямаркетингового застосування, а також літератури стосовно призначеного використання FemoSeal™ VCS.

Був проведений комплексний огляд опублікованої літератури за період з 1 вересня 2019 року по 31 серпня 2024 року. Доказова база включала в себе 29 досліджень з використанням пристрою FemoSeal™ VCS. На підставі отриманих свідчень було зроблено висновок про те, що при використанні за призначенням досліджуваний пристрій є безпечним та ефективним, а будь-які ризики або небажані побічні ефекти, які можуть бути пов'язані з пристроєм за нормальних умов використання, є прийнятними, якщо враховувати користь для пацієнта. Результати застосування досліджуваних пристроїв

відповідають очікуванім для цього типу пристроїв за умови використання за призначенням.

Потенційні небажані побічні ефекти, пов'язані з використанням FemoSeal™ VCS, включають небажані явища, що зазвичай спостерігаються при застосуванні альтернативних способів закриття артеріотомії, наприклад, кровотечу та гематому. Загалом частота небажаних явищ, про які повідомлялося при використанні FemoSeal™ VCS, подібна до частоти небажаних явищ, що спостерігаються при застосуванні ручної компресії та аналогічних пристроїв для закриття місця пункції судин. Зокрема, для кровотечі та гематоми показники частоти виникнення при застосуванні FemoSeal™ VCS є нижчими, ніж при застосуванні аналогічних пристроїв для закриття місця пункції судин. Кожне з повідомлених небажаних явищ, як в опублікованій літературі, так і в результатах післямаркетингового нагляду, було ідентифіковане раніше (див. **розділ 1.3**).

Наявні дані щодо клінічної безпечності та ефективності FemoSeal™ VCS дозволяють припустити, що переваги пацієнта від використання цього пристрою для закриття місця пункції судини переважають можливі ризики, якщо його використовувати відповідно до інструкції із застосування.

Як зазначено в попередніх розділах вище, дані щодо застосування пристрою FemoSeal™ VCS демонструють узгодженість між даними стосовно оцінюваного пристрою (наприклад, використання пристрою, показники безпечності та ефективності та клінічні переваги) і стосовно еквівалентних та подібних пристроїв.

Перехресний аналіз даних щодо безпечності не виявив жодних невідповідностей між наступними даними:

- Дані з публікацій, присвячених аналогічним пристроям
- Дані про оцінюваний виріб
- Дані, зазначені в документації з управління ризиками
- Дані, зазначені на маркуванні та/або в інструкціях із застосування (тобто, до уваги беруться тільки дані про залишкові ризики, призначені для користувачів пристрою).

Клінічна безпечність була продемонстрована низькою частотою ускладнень, про яку свідчили дані в опублікованій рецензованій клінічній літературі, результати клінічних досліджень, спонсорованих компанією, дані щодо післямаркетингового застосування та відсутність випадків вилучення з ужитку. Даних про незадовільні робочі характеристики в публікаціях, присвячених застосуванню FemoSeal™ VCS згідно з визначеним виробником цільовим призначенням, виявлено не було.



### 1.5 Можливі діагностичні або терапевтичні альтернативи

Ручна компресія традиційно застосовується для досягнення гемостазу в місці артеріотомії після катетеризації судин. Ручна компресія часто супроводжувалася обмеженням здатності пацієнта рухатися протягом тривалого часу (до 8 годин після процедури) та значним дискомфортом і тривалим перебуванням у лікарні. В результаті нещодавно проведеного систематичного огляду з'ясувалося, що середній час досягнення гемостазу в разі ручної компресії становив 20,8 хвилини.<sup>1</sup>

Альтернативою ручній компресії є зовнішні гемостатичні пристрої, принципом дії яких є механічна компресія місця артеріотомії. Ці пристрої не скорочують час до гемостазу або час до відновлення здатності пересуватися, але полегшують роботу медичних працівників, замінюючи ручну компресію механічною. Частота небажаних явищ при застосуванні механічної компресії аналогічна частоті небажаних явищ із застосуванням ручної компресії.

Пристрої для закриття місця пункції судин, такі як FemoSeal™ VCS, призначені для закриття артеріотомії. Використання таких пристроїв скорочує час до гемостазу і сприяє ранньому відновленню здатності пацієнта самостійно рухатися. Проведений нещодавно систематичний огляд даних, включаючи дані про 13 представлених на ринку пристроїв, свідчить про те, що середній час до досягнення гемостазу за допомогою пристрою для закриття місця пункції судини становить 5,4 хвилини. Середній час до гемостазу для окремих пристроїв для закриття місця пункції судин коливався від 1 хвилини (FemoSeal™ VCS) до 14 хвилин; для більшості пристроїв — від 4 до 10 хвилин.<sup>1</sup>

До поширених небажаних явищ, пов'язаних із закриттям місця артеріотомії із застосуванням ручної компресії, зовнішніх гемостатичних пристроїв або засобів для закриття місця пункції судини, належать гематома, кровотеча в місці доступу, псевдоаневризма, артеріовенозна фістула та інфекція. В результаті того ж систематичного огляду (34 рандомізованих контрольованих дослідження, 14 401 пацієнт) було виявлено, що частота небажаних явищ при застосуванні ручної компресії і використанні пристроїв для закриття місця пункції судин була аналогічною, за винятком того, що частота кровотеч при застосуванні пристроїв є трохи вищою.<sup>1</sup>

*1. Cox, T., Blair, L., Huntington, C., Lincourt, A., Sing, R., & Heniford, B. T. (2015). Systematic Review of Randomized Controlled Trials Comparing Manual Compression to Vascular Closure Devices for Diagnostic and Therapeutic Arterial Procedures. Surgical technology international, 27, 32–44.*



## 1.6 Профіль рекомендованого користувача та навчання

Призначеними користувачами системи для закриття місця пункції судини FemoSeal™ є лікарі, які отримали належну підготовку з виконання артеріального доступу через загальну стегнову артерію та закриття місця пункції в рамках ендovasкулярних процедур і пройшли спеціальний інструктаж із застосування пристрою FemoSeal™ від компанії Terumo Medical Corporation.

## 1.7 Відповідні гармонізовані та загальні стандарти

| Стандарт     | Поточний рік відповідності/<br>редакція | Опис                                                                                                                                     |
|--------------|-----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 11070    | 2014/AMD1:2018                          | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| EN ISO 11070 | 2014/A1:2018                            | Sterile single-use intravascular introducers, dilators and guidewires — Amendment 1                                                      |
| FDA Guidance | 20 травня 2021 р.                       | FDA Guidance: Testing and Labeling Medical Devices for Safety in Magnetic Resonance (MR) Environment                                     |
| ASTM F2052   | 2015                                    | Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment |
| ASTM F2213   | 2017                                    | Standard Test Method for Measurement of Magnetically Induced Torque on Medical Devices in the Magnetic Resonance Environment             |
| ASTM F2503   | 2020                                    | Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment                           |
| ASTM F2182   | 2019                                    | Standard Test Method for Measurement of Radio Frequency Induced Heating On or Near Passive Implants During Magnetic Resonance Imaging    |
| EN ISO 13485 | 2016/A11:2021                           | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |
| ISO 13485    | 2016                                    | Medical devices - Quality management systems - Requirements for regulatory purposes                                                      |

| Стандарт       | Поточний рік відповідності/<br>редакція | Опис                                                                                                                                                                     |
|----------------|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 14644-1    | 2015                                    | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| EN ISO 14644-1 | 2015                                    | Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration                                                  |
| ISO 14644-2    | 2015                                    | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| EN ISO 14644-2 | 2015                                    | Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration |
| ISO 14644-3    | 2019                                    | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| EN ISO 14644-3 | 2019                                    | Cleanrooms and associated controlled environments — Part 3: Test methods                                                                                                 |
| ISO 14698-1    | 2003                                    | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| EN ISO 14698-1 | 2003                                    | Cleanrooms and associated controlled environments — Biocontamination control — Part 1: General principles and methods                                                    |
| ISO 14698-2    | 2003/TC1:2004                           | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| EN ISO 14698-2 | 2003/TC 1:2004                          | Cleanrooms and associated controlled environments — Biocontamination control — Part 2: Evaluation and interpretation of biocontamination data                            |
| USP <788>      | H/3                                     | PARTICULATE MATTER IN INJECTIONS                                                                                                                                         |

| Стандарт               | Поточний рік відповідності/<br>редакція | Опис                                                                                                                 |
|------------------------|-----------------------------------------|----------------------------------------------------------------------------------------------------------------------|
| EU Pharmacopeia 2.9.19 | H/3                                     | Particulate Contamination: Sub-Visible Particles                                                                     |
| IEC 62366-1            | 2015                                    | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN 62366-1             | 2015                                    | Medical devices — Part 1: Application of usability engineering to medical devices                                    |
| EN ISO 14971           | 2019/A11:2021                           | Medical devices — Application of risk management to Medical devices                                                  |
| ISO 14971              | 2019                                    | Medical devices — Application of risk management to Medical devices                                                  |
| ASTM F1980             | 2016                                    | Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices                                  |
| EN ISO 10993-1         | 2020                                    | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| ISO 10993-1            | 2018                                    | Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process           |
| EN ISO 10993-2         | 2006                                    | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| ISO 10993-2            | 2006                                    | Biological evaluation of medical devices — Part 2: Animal welfare requirements                                       |
| EN ISO 10993-3         | 2014                                    | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| ISO 10993-3            | 2014                                    | Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity |
| EN ISO 10993-4         | 2017                                    | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood                     |

| Стандарт        | Поточний рік відповідності/ редакція | Опис                                                                                                           |
|-----------------|--------------------------------------|----------------------------------------------------------------------------------------------------------------|
| ISO 10993-4     | 2017                                 | Biological Evaluation of Medical Devices- Part 4: Selection of tests for interactions with blood               |
| EN ISO 10993-5  | 2009                                 | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                             |
| ISO 10993-5     | 2009                                 | Biological evaluation of medical devices – Part 5: Tests for in vitro cytotoxicity                             |
| EN ISO 10993-6  | 2016                                 | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                  |
| ISO 10993-6     | 2016                                 | Biological evaluation of medical devices - Part 6: Tests for local effects after implantation                  |
| EN ISO 10993-10 | 2023                                 | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                 |
| ISO 10993-10    | 2021                                 | Biological evaluation of medical devices —Part 10: Tests for irritation and skin sensitization                 |
| EN ISO 10993-11 | 2018                                 | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                |
| ISO 10993-11    | 2017                                 | Biological evaluation of medical devices — Part 11: Tests for systemic toxicity                                |
| EN ISO 10993-12 | 2021                                 | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                 |
| ISO 10993-12    | 2021                                 | Biological evaluation of medical devices — Part 12: Sample preparation and reference materials                 |
| EN ISO 10993-17 | 2009                                 | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances |
| ISO 10993-17    | 2002                                 | Biological evaluation of medical devices — Part 17: Establishment of allowable limits for leachable substances |

| Стандарт        | Поточний рік відповідності/ редакція | Опис                                                                                                                                                                         |
|-----------------|--------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ISO 10993-18    | 2020/A1:2022                         | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-18 | 2020/A1:2022                         | Biological evaluation of medical devices — Part 18: Chemical characterization of medical device materials within a risk management process                                   |
| EN ISO 10993-23 | 2021                                 | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ISO 10993-23    | 2021                                 | Biological evaluation of medical devices - Part 23: Tests for irritation                                                                                                     |
| ASTM F2382      | 2018                                 | Standard Test Method for Assessment of Circulating Blood-Contacting Medical Device Materials on Partial Thromboplastin Time (PTT)                                            |
| ASTM F756       | 2017                                 | Standard Practice for Assessment of Hemolytic Properties of Materials                                                                                                        |
| USP <85>        | H/3                                  | [Bacterial Endotoxins Test. (Sterility)]                                                                                                                                     |
| USP <161>       | H/3                                  | Medical Device - Bacterial Endotoxin and Pyrogen Tests                                                                                                                       |
| ANSI/AAMI ST72  | 2019                                 | Bacterial endotoxins - Test methods, routine monitoring, and alternatives to batch testing                                                                                   |
| EN ISO 11135    | 2014/A1:2019                         | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development, Validation and Routine Control of a Sterilization Process for Medical Devices |
| ISO 11135       | 2014/A1:2018                         | Sterilization of Health Care Products – Ethylene Oxide – Part 1: Requirements for Development,                                                                               |

| Стандарт       | Поточний рік відповідності/ редакція | Опис                                                                                                                                                            |
|----------------|--------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                |                                      | Validation and Routine Control of a Sterilization Process for Medical Devices                                                                                   |
| EN ISO 10993-7 | 2008/A1:2022                         | Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals                                                                       |
| ISO 10993-7    | 2008/A1:2019                         | Biological evaluation of medical devices — Part 7: Ethylene oxide                                                                                               |
| EN 556-1       | 2024                                 | Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices |
| EN ISO 11737-1 | 2018/A1:2021                         | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| ISO 11737-1    | 2018/A1:2021                         | Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products                           |
| EN ISO 11138-1 | 2017                                 | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| ISO 11138-1    | 2017                                 | Sterilization of health care products - Biological indicators - Part 1: General requirements                                                                    |
| EN ISO 11138-2 | 2017                                 | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| ISO 11138-2    | 2017                                 | Sterilization of health care products — Biological indicators — Part 2: Biological indicators for ethylene oxide sterilization processes                        |
| EN ISO 15223-1 | 2016                                 | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |
| ISO 15223-1    | 2016                                 | Medical device – Symbols to be used with medical device labels, labeling and information to be supplied – Part 1: General requirements                          |

| Стандарт          | Поточний рік відповідності/ редакція | Опис                                                                                                                                    |
|-------------------|--------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| EN 1041           | 2008/A1:2013                         | Information supplied by the manufacturer of medical devices                                                                             |
| EN ISO 11607-1    | 2020/A1:2023                         | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems |
| ISO 11607-1       | 2019/A1:2023                         | Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for Materials, Sterile Barrier Systems and Packaging Systems |
| EN ISO 11607-2    | 2020/A1:2023                         | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes      |
| ISO 11607-2       | 2019/A1:2023                         | Packaging for Terminally Sterilized Medical Devices – Part 2: Validation requirements for forming, sealing, and assembly processes      |
| ASTM D4169        | 2016                                 | Standard Practice for Performance Testing of Shipping Containers and Systems                                                            |
| ASTM F1886/F1886M | 2016                                 | Standard Test Method for Determining Integrity of Seals for Flexible Packaging by Visual Inspection                                     |
| ASTM F2825        | 2018                                 | Standard Practice for Climatic Stressing of Packaging Systems for Single Parcel Delivery                                                |
| ASTM F2096        | 2011 (R 2019)                        | Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)                            |
| ASTM F88/F88M     | 2015                                 | Standard Test Method for Seal Strength of Flexible Barrier Materials                                                                    |
| MDCG 2021-24      | 2021                                 | Guidance on classification of medical devices                                                                                           |
| MDCG 2020-3       | 2020                                 | Guidance on significant changes regarding the transitional provision under Article 120 of the MDR                                       |

| Стандарт       | Поточний рік відповідності/ редакція | Опис                                                                                                                                                                               |
|----------------|--------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                |                                      | with regard to devices covered by certificates according to MDD or AIMDD                                                                                                           |
| MDCG 2020-8    | 2020                                 | Post-market clinical follow-up (PMCF) Evaluation Report Template A guide for manufacturers and notified bodies                                                                     |
| MDCG 2020-7    | 2020                                 | Post-market clinical follow-up (PMCF) Plan Template A guide for manufacturers and notified bodies                                                                                  |
| MDCG 2020-6    | 2020                                 | Regulation (EU) 2017/745: Clinical evidence needed for medical devices previously CE marked under Directives 93/42/EEC or 90/385/EEC                                               |
| MDCG 2019-9 v1 | 2022                                 | Summary of safety and clinical performance A guide for manufacturers and notified bodies                                                                                           |
| MDCG 2019-8 v2 | 2020                                 | Guidance document Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices |
| MDCG 2020-15   | 2020                                 | MDCG Position Paper on the use of the EUDAMED actor registration module and of the Single Registration Number (SRN) in the Member States                                           |
| MDCG 2021-11   | 2021                                 | Guidance on Implant Card – ‘Device types’                                                                                                                                          |
| MDCG 2021-19   | 2021                                 | Guidance note integration of the UDI within an organisation’s quality management system                                                                                            |
| MDCG 2018-1 v4 | 2021                                 | Guidance on BASIC UDI-DI and changes to UDI-DI                                                                                                                                     |
| MDCG 2019-2    | 2019                                 | Guidance on application of UDI rules to device-part of products referred to in Article 1(8), 1(9) and 1(10) of Regulation 745/2017                                                 |
| MDCG 2019-1    | 2019                                 | MDCG guiding principles for issuing entities rules on Basic UDI-DI                                                                                                                 |



| Стандарт            | Поточний рік відповідності/ редакція | Опис                                                                                                                                                                                                                                                          |
|---------------------|--------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| MDCG 2018-7         | 2018                                 | Provisional considerations regarding language issues associated with the UDI database (Annex VI, Part A Section 2 and Part B of the Medical Device Regulation (EU) 2017/745 (MDR) and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746 (IVDR)) |
| MDCG 2018-6         | 2018                                 | Clarifications of UDI related responsibilities in relation to Article 16 of the Medical Device Regulation (EU) 2017/745 and the In-Vitro Diagnostic Medical Device Regulation (EU) 2017/746                                                                   |
| MDCG 2018-4         | 2018                                 | MDCG 2018-4 Annex: UDI database Definitions/Descriptions and formats of the UDI core elements for systems or procedure packs                                                                                                                                  |
| MDCG 2018-3 v1      | 2020                                 | Guidance on UDI for systems and procedure packs                                                                                                                                                                                                               |
| MDCG 2021-25        | 2021                                 | Regulation (EU) 2017/745 - application of MDR requirements to 'legacy devices' and to devices placed on the market prior to 26 May 2021 in accordance with Directives 90/385/EEC or 93/42/EEC                                                                 |
| Meddev 2.12-2 Rev 2 | 2012                                 | Guidance document Medical devices - Market surveillance - Post Market Clinical Follow-up studies - MEDDEV 2.12/2 rev.2                                                                                                                                        |

## 2.0 БІБЛІОГРАФІЯ

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### 3.0 ХРОНОЛОГІЯ РЕДАКЦІЙ ДОКУМЕНТА

| Номер редакції<br>SSCP     | Дата виходу        | Опис зміни                                                  | Редакція підтверджена<br>уповноваженим органом                                                                                                                                                                                                                                                                                                                  |
|----------------------------|--------------------|-------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SSCP-FS-2022               | 20 січня 2023 р.   | Початкова редакція після сертифікації MDR CE                | <input checked="" type="checkbox"/> Так<br>Мова документу, редакція якого перевірялася: English<br><input type="checkbox"/> Ні (застосовується лише для імплантованих пристроїв класу Іа або деяких пристроїв класу Іб (MDR, Стаття 52 (4) 2-й параграф), для яких SSCP ще не підтверджений уповноваженим органом)<br><input type="checkbox"/> Інше (пояснити): |
| SSCP-FS-2023 –<br>Версія 1 | 15 березня 2024 р. | Оновлено за період з 1 січня 2019 р. по 31 грудня 2023 р.   | <input checked="" type="checkbox"/> Так<br>Мова документу, редакція якого перевірялася: English<br><input type="checkbox"/> Ні (застосовується лише для імплантованих пристроїв класу Іа або деяких пристроїв класу Іб (MDR, Стаття 52 (4) 2-й параграф), для яких SSCP ще не підтверджений уповноваженим органом)<br><input type="checkbox"/> Інше (пояснити): |
| SSCP-FS-2024<br>Редакція 1 |                    | Оновлено за період з 1 вересня 2019 р. по 31 серпня 2024 р. | <input type="checkbox"/> Так<br>Мова документу, редакція якого перевірялася: English<br><input type="checkbox"/> Ні (застосовується лише для імплантованих пристроїв класу Іа або деяких пристроїв класу Іб (MDR, Стаття 52 (4) 2-й параграф), для яких SSCP ще не                                                                                              |

|                            |               |                                                         |                                                                                                                                                                                                                                                                                                                                                                                                 |
|----------------------------|---------------|---------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                            |               |                                                         | підтверджений<br>уповноваженим органом)<br><br><input type="checkbox"/> Інше (пояснити):                                                                                                                                                                                                                                                                                                        |
| SSCP-FS-2024<br>Редакція 2 | June 20, 2025 | Переглянуто на основі<br>запитів NSAI щодо<br>валідації | <input checked="" type="checkbox"/> Так<br>Мова документу, редакція<br>якого перевірялася: English<br><br><input type="checkbox"/> Ні (застосовується лише<br>для імплантованих пристроїв<br>класу Іа або деяких<br>пристроїв класу Іb (MDR,<br>Стаття 52 (4) 2-й параграф),<br>для яких SSCP ще не<br>підтверджений<br>уповноваженим органом)<br><br><input type="checkbox"/> Інше (пояснити): |